Pediatric and Developmental Pathology – Two recent articles show the benefits of molecular testing in pediatric cases of thyroid lesions, and, as editor Miguel Reyes-Múgica, MD, states, "provide a proven panel of molecular tests to do just that." Pediatric thyroid lesions tend to be cancerous more often than those found in adults, but as the first article, "Integrating Molecular Testing in the Diagnosis and Management of Children with Thyroid Lesions," acknowledges, detecting thyroid nodules, found in 1–2 percent of children, can be difficult. Even with the aid of cytologic evaluation, 10–40 percent of pediatric thyroid lesion (TL) diagnoses are inconclusive.

Many times children with these undetermined diagnoses are treated with hemithyroidectomy, and, if cancer is found, completion thyroidectomy. Having multiple surgeries increases both cost and risk of complications as a result of treatment. The writers recognize the need to address the molecular alterations present in pediatric TL.

The authors tested 27 thyroid carcinomas from patients aged 10 to 19 years for alterations common in adult TL, including BRAF V600E mutation, RET fusions, and TERT promoter mutations. They searched for additional targets in mutation-negative cases by using a next-generation sequencing (NGS) mutation panel. Results showed 12 classic papillary thyroid carcinomas (PTCs), 13 follicular variant PTCs, one medullary thyroid carcinoma, and one follicular carcinoma, with 14 showing lymph node involvement, and 13 showing lymphovascular invasion. Ten cases showed the BRAF V600E mutation, and six showed RET fusions. The team concluded that molecular abnormalities are common in pediatric TLs, ultimately showing a need for increased molecular testing in these cases.

As author Dolores López-Terrada, MD, PhD, says, "Thyroid nodules are often diagnosed in children; however, our understanding of the underlying genetic alterations of pediatric thyroid lesions and how they compare to those seen in adults, is limited. The study specifically demonstrates the utility of molecular testing of fine needle aspiration biopsies, and how this information may improve clinical management and avoid surgical procedures in cases showing atypia of uncertain significance. Characterization of the genetic defects underlying thyroid lesions diagnosed in children might also be prognostically relevant, such as in tumors seen in adults carrying specific mutations associated with higher recurrence rates, and even be

indicated for the selection of targeted therapies in some patients."

Similarly, the purpose of the study described in the second article, "Molecular Characterization of Sporadic Pediatric Thyroid Carcinoma with the DNA/RNA ThyroSeq v2 Next-Generation Sequencing Assay," was to determine whether the researchers' 60-gene DNA/RNA ThyroSeq v2 next-generation sequence (NGS) assay could identify more genetic markers, such as gene fusions in sporadic pediatric differentiated thyroid carcinomas (DTC), than standard testing alone.

The study showed that the ThyroSeq v2 NGS increased the identification rate of molecular alterations by 27 percent compared to standard testing. This testing could be highly beneficial for efficiency in pediatric thyroid lesion cases. As author Jennifer Picarsic described, "Children identified with thyroid lumps are typically biopsied with a fine needle. In most cases, the cells viewed under the microscope are benign or malignant. However, in cases where the result is indeterminate/inconclusive, the patient may need a repeat biopsy or have the lump surgically removed in the operating room. If the lump is cancerous, then the child has to go back to the operating room to remove the other thyroid lobe. Thus, by having an additional upfront test, as with the ThyroSeq panel, children with indeterminate nodules may benefit from having a more personalized treatment plan and prevent additional procedures. Our findings support the use of broader genetic testing in pediatric thyroid nodule evaluation, which may aid future management recommendations and better insight into the natural history and basic biology of sporadic pediatric thyroid cancer."

In addition, Picarsic explained that "while thyroid cancer in the pediatric population is generally rare, increased numbers of children present with thyroid lumps/nodules that may harbor a greater risk of malignancy as compared to adults. Pediatric thyroid cancer was once thought to have lower rates of molecular alterations as compared to adult thyroid cancer. However, this may not be entirely accurate. We investigated pediatric thyroid cancers using a new next-generation sequencing test called ThyroSeq that looks at a larger number of cancer-associated mutations. We found previously unrecognized genetic changes in a small cohort of pediatric thyroid cancer patients."

Full text of the articles, " Integrating Molecular Testing in the Diagnosis and Management of Children with Thyroid Lesions " and " Molecular Characterization of Sporadic Pediatric Thyroid Carcinoma with the DNA/RNA ThyroSeq v2 Next-Generation Sequencing Assay ," is available in the current issue

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