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Clinicopathological, Molecular and Genetic Characteristics of Thymic Tumors in Multiple Endocrine Neoplasia 1 Syndrome

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BACKGROUND: Thymic carcinoids associated with multiple endocrine neoplasia 1 (MEN1) are rare yet highly aggressive tumors that have a high mortality rate. The goal of this study was to analyze the clinicopathological, genetic, and molecular features of thymic tumors in MEN1 patients at our institution.

METHODS: In our longstanding prospective natural history study, we identified thymic tumors in 14/350 (4%) germline MEN1mutation patients (12 carcinoids, 2 thymomas). We evaluated demographic characteristics, MEN1 related diseases as well as recurrence, and overall survival. We analyzed tumor histopathology and isolated DNA to evaluate for loss of heterozygosity at the MEN1 locusand performed RNA sequencing to help further understand the characteristics of the tumors.

RESULTS: Thymic carcinoids occurred exclusively in men; 2 females had thymomas. Median age of diagnosis was 43 years old (range 29-65), 7/14 (50%) of the patients were smokers, and the mean tumor diameter was 7.18 cm (range 2.5-15 cm). ACTH production was not detected in any of the cases. Tumor recurrence occurred in 8 patients. Familial clustering was identified in 6 patients within 5 families. MEN1 mutations did not show any specific clustering within the MEN1 gene but a preponderance of protein truncating mutations was observed.

Loss of heterozygosity analysis is currently in progress. RNA-sequencing has helped to determine subtypes of MEN1-associated thymic tumors as well as to identify potential therapeutic targets for small molecule inhibitors.

CONCLUSION: We present the clinicopathological, genetic, and molecular features of 14 thymic tumors in MEN1 patients. Familial clustering of thymic tumors within MEN1 families suggests the need for increased surveillance in affected male family members. Histopathological analysis and characterization of RNA-sequencing data have helped to determine subtypes of MEN1-associated thymic tumors as well as to identify potential therapeutic targets for small molecule inhibitors.