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Tumor Prevalence and Clinical Follow-Up of Brazilian Patients with Li-Fraumeni Syndrome Associated with TP53 p.R337H Mutation: A Single Center Experience

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Background: TP53 p.R337H germline mutation is highly prevalent among individuals from South and Southeast Brazil; mainly in pediatric adrenocortical tumours (ACTs). The prevalence Li-Fraumeni Syndrome (LFS) spectrum, clinical outcomes and tumor occurrence in relatives carrying has not been fully investigated.

Patients and Methods: Medical records of all LFS and LFL patients with p.R337H were reviewed and tumor profile data, clinical characteristics and outcomes assessed. Tumor penetrance in familial carriers was also evaluated.

Results: 47 of 43 families, female (70%), with LFS due to TP53 p.R337H mutation. Maternal inheritance occurred in 72%. ACT in the pediatric group was diagnosed in 57%; (median age = 2 years), in adult group ACC in 23%; (median age= 29.5 years), breast cancer (11%; median age = 41 years), sarcoma (6%; median age = 50.3 years) and choroid plexus carcinoma (CPC) (2%; median age = 18 years). Children did not develop the second tumor and 11% (n=3) died due to complications related to the initial tumor *(median follow-up time of 81.5 months, range= 3-378 months)*. Among adult with ACC all presented aggressiveness histologic and clinical criteria at diagnosis and 82% of patients died *(median follow-up time of 19 months, range = 1-69 months)*. The adult patients that presented a second primary tumor (n = 4; 9%) have had breast cancer, sarcoma or ACC as their first syndromic manifestation. The second primary tumors were bronchi alveolar lung cancer, ACC, uterine cervical carcinoma and fibrosarcoma, diagnosed 8, 18, 26 and 36 months after diagnosis of first primary tumor, respectively. Among these 4 patients, two patients died (*median follow-up time of 60 months, range= 8 to 218 months).* Two cases of adrenocortical tumor in the same family were observed only once - they were second-degree cousins and one presented ACT in infancy and had an optimal evolution *(overall survival = 378 months)* and the other presented ACC in adulthood and had a poor outcome *(overall survival =6 months).* Cancer screening in familial asymptomatic carriers (n = 71) according to Toronto Protocol identified only three malignant neoplasms in three different carriers.

Conclusions: This study showed that TP53 p.R337H mutation is associated with ACT in the pediatric group but also brings new insights such as the occurrence of others tumors of LFS spectrum, the rare occurrence of multiple tumours, the predominance of maternal inheritance and mostly the difference in aggressiveness of adrenocortical tumours depending on the age group in which it was diagnosed. The pronounced intra and interfamilial phenotypic diversity raises the need to understand the other events that, added to the presence of this mutation justify these findings.

Biography:

Dr. Maria CandidaBarisson Villares Fragoso Professor of the Clinical Hospital of the Faculty of Medicine of the University of São Paulo, Head of the Suprarenal Unit of the Department of Endocrinology and Metabolism of HCFMUSP, Medical Researcher at the Laboratory of Hormones and Molecular Genetics LIM / 42, Graduated in Medicine from the Pontifical Catholic University of Campinas in 1989. Obtained her PhD in Endocrinology and Metabology, Faculty of Medicine, University of São Paulo in 1999. Post-doctorate in Endocrinology and Metabology, Faculty of Medicine, University of São Paulo in 2002. She was a Senior Researcher at University Hospital Center Research Center (CHUM) at the Laboratory of Endocrine Pathophysiology Montreal / Canada, CNPq Senior Scholarship in 2009. And was a Professor in Endocrinology and Metabology, Faculty of Medicine, University of São Paulo in 2011. CNPq Scholarship-Productivity in Research (2013-2019).

She is presently member of the Brazilian Society of Endocrinology and Metabology and Effective Member of the Endocrine Society (USA), European Network for the Study of Adrenal Tumors ENSAT and also for the A5Adrenal Network American Australian Asian Adrenal Alliance.