Abstract citation ID: bvac150.273

Adrenal

RF09 | PSUN29

Evidence for a Founder Effect of SDHB Exon 1 Complete Deletion in Brazilian Patients with Paraganglioma

Gustavo F. Fagundes, MD, Madson Q Almeida, MD, PhD, Lucas Santana, PhD, Felipe Castro, PhD, Ana Caroline Afonso, Janaina Petenuci, MD, Mariana Funari, PhD, Augusto G Guimarães, Elaine V Sales, Ana Vieites, MD, PhD, Gabriela Sanso, MD, PhD, Felipe L Ledesma, MD, PhD, Sheila Siqueira, MD, PhD, Maria Adelaide A Pereira, MD, PhD, Fabio Y Tanno, MD, PhD, Vitor Srougi, MD, PhD, Jose L Chambo, MD, PhD, Carolina R Victor, MD, PhD, Marcela S. Ferrari, MD, PhD, Fernando M. Coelho, MD, PhD, Silvia C Soares, MD, PhD, Ana Claudia Latronico, MD, PhD, Berenice B Mendonca, MD, PhD, Maria Candida BV Fragoso, MD, PhD, and Ana O Hoff, MD, PhD

Background: Pheochromocytomas and paragangliomas (PPGLs) have the highest degree of heritability among endocrine tumors. Currently, ~40% of PPGL individuals have a genetic germline pathogenic variant and exist at least 12 different genetic syndromes related to these tumors. Pathogenic variants in the Succinate Dehydrogenase Complex Subunit B (SDHB) gene account for about 10% of PPGL cases. Moreover, SDHB pathogenic variants are the most well-established risk factor to predict metastatic disease (40%-50% of cases). Germline SDHB large deletions are very rare worldwide, but SDHB exon 1 deletion has been reported in patients with PPGLs from Portugal and Spain. Indeed, a putative founder effect for SDHB exon 1 deletion was suggested in PPGL patients from Iberian Peninsula. **Aim:** To investigate a putative founder effect for SDHB exon 1 deletion. **Methods:** Eighteen unrelated Brazilian patients with germline heterozygous SDHB pathogenic variants were included. Additionally, two unrelated individuals with SDHB exon 1 complete deletion from Argentina were studied. SDHB pathogenic variants were investigated by automated SAGER sequencing, multiplex ligation-dependent probe amplification (SALSA MLPA Probemix P226 SDH) and/or high-throughput sequencing. Five SDHB flanking microsatellite markers at chromosome 1p (D1S2697, GATA29A05, D1S2826, D1S2644, and D1S199) were used to investigate if patients carrying this deletion have a common origin. Haplotypes were reconstructed using the PHASE algorithm (v. 2.1). A control group comprising 26 unrelated Brazilian individuals was also studied. **Results:** Among 18 Brazilian patients with germline SDHB pathogenic variants, heterozygous SDHB exon 1 complete deletion was identified in 6 of them (33% of the cases). The remaining 12 patients presented intragenic SDHB pathogenic variants without hotspot location. All Brazilian index patients with SDHB exon 1 deletion presented with paraganglioma, located mostly in the abdomen (4 abdominal; one thoracic; two head and neck and one colonic). Median age was 31.5 years and metastatic disease occurred in 3 (50%) of them. Haplotype analysis showed that 4 apparently unrelated Brazilian patients (4 out of 6 cases, 67%) shared a common allele (SDHB-GATA29A05-D1S2826-D1S2644-D1S199 | SDHB-186-130-213-102), which was not seen in chromosomes without the SDHB exon 1 deletion (p= 0.01). The two cases from Argentina did not have this haplotype, suggesting that SDHB exon 1 deletion in Argentina have a different origin. **Conclusion:** SDHB exon 1 complete deletion was the most frequent SDHB defect in our cohort. Our findings indicate a founder effect for SDHB exon 1 complete deletion in Brazilian patients with paraganglioma.

Support: Sao Paulo Research Foundation (FAPESP) grant 2019/15873-6

Presentation: Saturday, June 11, 2022 1:24 p.m. - 1:29 p.m., Sunday, June 12, 2022 12:30 p.m. - 2:30 p.m.