The Abstract book

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O-073 Brainstem anomalies in stillbirth: a neuropathological and genetic preliminary study

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Objective: Central nervous system (CNS) abnormalities represent a common cause of stillbirth (SB), especially in the third trimester of pregnancy, being detected in more than 1/3 cases subjected to fetal autopsy and post-mortem, or in utero, brain magnetic resonance imaging (MRI). Brainstem nuclei are implicated in the control of crucial physiological functions during fetal life such as swallowing, breathing movements, heart rate, and blood pressure.
The "brainstem hypothesis" implies that dysfunction of such anatomical regions may increase vulnerability to sudden infant death syndrome (SIDS)/sudden unexplained death in childhood (SUDC). This preliminary study combines neuropathological and genetic investigations, under the hypothesis that SIDS/SUDC and SB may represent distinct etiological entities although in a genotypic and phenotypic continuum from fetal life to childhood.

Methods: We investigated a subset of 29 stillbirths (18 males and 11 females) showing prominent brainstem anomalies, such as arcuate nucleus and pre-Botzinger complex hypoplasia, by whole-exome sequencing (WES). Samples were part of archival material collected from the Lino Rossi Research Center between 2008 and 2022. Histopathological analysis was performed on

serial sections. All but one fetal loss occurred after 28 gestational weeks (mean: 38.05; range: 27-41.7). Genomic DNA was extracted from postmortem formalin-fixed paraffin-embedded brain tissues and matched normal tissues as controls (thymus or thyroid). After deep sample quality evaluation, DNA samples underwent WES by using the Human Core Exome kit with Mitochondrial Panel (Twist Bioscience) on a Novaseq6000 platform (Illumina).

Results: The bioinformatic analysis, still ongoing, was focused on genetic variants with a minor allele frequency below 5%, located within exonic and splicing regions and related to abnormal brainstem morphology according to the Human Phenotype Ontology (HPO) and related interactome data.

Conclusion: This study will help to identify the correlation of neuropathological anomalies with genetic bases and their intriguing overlaps in SIDS/SUDC.