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POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: EM RESEARCH RELATED TO MEDICINE

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Abstract P-43: Effect of Glucocerebrosidase Dysfunction on the Pool of Plasma Exosomes of Patients with Gaucher Disease

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Background: Extracellular vesicles (EVs) are small membrane vesicles released from different types of cells. EVs are found in many human biological fluids. Exosomes are a subtype of EVs that are released by the fusion of multivesicular bodies with the plasma membrane. This type of vesicles is characterized by specific exosomal markers. Exosomes extracted from peripheral body liquids could have specific properties associated with different physiological conditions as well as human disorders, including neurodegenerative diseases.
Gaucher disease (GD) – is the most common form of lysosomal storage disorders caused by mutations in the glucocerebrosidase (*GBA*) gene. Lysosome functionality is critical for the regulation of extracellular vesicle secretion and content. In model animals, the inhibition of glucocerebrosidase has been shown to increase the secretion of extracellular vesicles in brain tissues. Amount evaluation of EVs and their size in the biological fluids of patients with GD has not been early performed; therefore, it is unknown whether lysosomal dysfunction found in GD patients influences the plasma pool of EVs. The aim of this study was to evaluate the amount of blood plasma EVs in patients with GD and their characterization for morphology and size.

Methods: EVs were isolated from the blood plasma of 8 GD patients and 8 controls by ultracentrifugation, and were characterized using cryo-electron microscopy (cryo-EM), nanoparticle tracking analysis (NTA), and dynamic light scattering (DLS). Also, the presence of exosomal markers CD9, CD63, CD81, and HSP70 was analyzed by flow cytometry and western blot.
Results: Here, it was first shown an increased proportion of exosome fraction in EVs from plasma of GD patients compared to controls by DLS and cryo-EM ($p<0.001$) that was confirmed by mode size detected by NTA ($p<0.02$). Moreover, an increased number of double and multilayer vesicles in plasma EVs from GD patients was demonstrated by cryo-EM. We also detected an increase in the expression of exosomal markers on the surface of vesicles from the blood plasma of patients with GD compared to controls.
Conclusion: Here, we firstly report that the exosomes obtained from the blood plasma of GD patients have a larger size and altered morphology. Thus, we have shown that lysosomal dysfunction in GD patients leads to a striking alteration of blood plasma extracellular vesicle pool.

Key Words: cryo-EM • extracellular vesicles • exosomes • Gaucher disease

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