P-054 - EYE PATHOLOGY IN MUCOPOLYSACCHARIDOSIS TYPE I AND EFFECTS OF ENZYME REPLACEMENT THERAPY

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INTRODUCTION: Mucopolisaccharidoses type I (MPS-I) is an lysosomal storage disorder caused by deficiency in alpha-L-iduronidase (IDUA), which is involved in the degradation of glycosaminoglycans (GAG). Accumulation of GAG in ocular tissues can cause corneal opacity or neurosensory complications. Nevertheless, the time course and effect of intravenous enzyme replacement (ERT) in MPS-I are undetermined. ***OBJECTIVE:*** To investigate the ocular alterations overtime as well as the effect of ERT on eye disease in MPS-I mice. To describe the histological findings in the cornea from a MPS-I patient treated for over a decade with ERT. ***MATERIALS AND METHODS:*** Eyes were obtained from 2, 6 and 8 months-old normal and MPS-I mice. A group of MPS-I mice received ERT (1.2mg/kg of laronidase®) every 2 weeks from 6 to 8 months. Paraffin sections were stained with Hematoxylin-eosin/Alcian-blue, for GAG visualization, or picrosirius-red, for collagen structure. Corneal lesion was evaluated according to a scale grade of alteration. Thickness of cornea and retinal nuclear layer were measured overtime and compared with age-matched controls. Biochemical and histological evaluation was performed in the cornea from a MPS-I patient after 13 years of ERT. ***RESULTS:*** Cornea from MPS-I mice showed GAG accumulation and structural alteration from two months ($p<0.05$), with a lesions score greater than normal mice. Collagen structure seemed altered at 8 months, but only a trend towards reduction in the MPS I mice was observed. A progressive loss of photoreceptors was found in the outer nuclear layer, starting at 6 months (24% reduction;$p<0.01$). Mice treated with ERT did not show improvements in eye pathology. A similar finding was observed in the cornea from a MPS-I patient. Her cornea still presented vacuoles with GAG accumulation within distended stromal cell and undetectable IDUA activity, despite ERT. ***CONCLUSION:*** We provide data on the time course of ocular alteration in MPS I mice. Corneal alterations occur early, while retinal pathology shows up later in life, both of which probably affect the visual function. Our data suggest that ERT is ineffective to correct the ocular alterations in MPS-I mice and patients, indicating that the enzyme does not access the tissue at appreciable levels.