Tonsillar pathology in 7-year-old mucopolysaccharidosis type II female patient

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The aim of our study was to explore tonsillar tissue pathology in a female patient with mucopolysaccharidosis type II (MPS II). Surgically obtained nasopharyngeal and palatine tonsillar tissues were analyzed histologically, immunohistochemically and ultrastructurally.

Extensive storage changes were observed in follicular germinal center histiocytes. We have also identified an additional population of foamy cells in the tonsillar paracortex. These cells likely correspond to interdigitating dendritic cells. This abnormality may impact mucosal T-cell mediated antigen processing in patients with MPS II.

Objectives
- Mucopolysaccharidosis type II (MPS II, Hunter syndrome,) is a multisystemic progressive lysosomal storage disorder associated with accumulation of glycosaminoglycans (GAGs).
- Multisystemic manifestations of MPS II include:
  - craniofacial dysmorphism
  - musculoskeletal involvement, joint contractures
  - hepatosplenomegaly, inguinal or umbilical hernias
  - cognitive impairment
- ENT symptoms are very common in MPS II and include:
  - otological involvement - recurrent OMA, OME, progressive hearing loss
  - adenotonsillar hypertrophy
  - progressive airway obstruction

Aims
- Histopathological and ultrastructural evaluation of adenoid and tonsillar lymphoid tissue from a female MPS II patient

Case report
- A 7 yr. old girl, with a neuromatonic form of MPS II due to extremely skewed inactivation of the X-chromosome
- Urinary excretion of heparan and dermatan sulphates were increased (60.5–65.7 g/mol creatinine; controls < 15.5)
- The enzymatic activity of iduronate 2-sulfatase (IDS) was markedly decreased in the patient’s leukocytes (0.46 nmol/4 h/mg, control range: 28.1–70.4 nmol/4 h/mg)
- Heterozygous mutation c.1403G>A (p.Arg468Gln) was identified in the IDS gene
- Adenoidectomy was performed at the age of 2 years
- Hearing impairment was diagnosed and hearing aids were recommended at the age of 4 years
- Aprena-Hypopnea index (AHI) 13.8 was identified by a sleep study at the age of 6.5 years
- Subsequent adenotonsillectomy significantly improved the patient’s sleep parameters

Results
Histopathological, immunohistochemical and ultrastructural analyses of the tonsillar tissue are summarized in Fig.2.

H&E

anti-CD68 (germinal center histiocytes)

anti-CD63 (paracortical interdigitating dendritic cells - IDCs)

(A, B) hematoxylin-eosin (H&E) stain highlights the vacuolated follicular germinal center (outlined by dashed line) histiocytes/macrophages (black arrows in B, image shown as B corresponds to the rectangle in A)

(C,D) vacuolated follicular germinal center (outlined by dashed line) histiocytes/macrophages are highlighted by anti-CD68 antibody (image shown as D corresponds to the rectangle in C)

(E) electron microscopy of a follicular germinal center histiocyte/macrophage with cytoplasm containing partly cleared membrane-bound vacuoles with finely granular contents

(F,G) vacuolated paracortical interdigitating dendritic cells (IDCs) are highlighted by anti-CD63 antibody (image shown as G corresponds to the rectangle in F). The dashed line in F outlines the follicular germinal center. C and F images are taken from serial histological sections and show the same follicle

(H) electron microscopy shows IDCs with cytoplasm containing not only partly cleared membrane-bound vacuoles with finely granular contents but also occasional zebra body-like structures (black arrow in the inset)

Scale bars = 100 μm (A, C, F); 2 μm (E, H)

Conclusion
Morphological studies of the MPS II tonsillar lymphoid tissues revealed extensive storage changes in follicular germinal center histiocytes and also in paracortical interdigitating dendritic cells.

We defined the tonsillar tissue pathology and provide important structural cues for any future studies aimed at mucosal antigen processing in MPS II.