CANADIAN SYMPOSIUM ON LYSOSOMAL DISEASES

OCTOBER 5-6, 2018

ACCEPTED ABSTRACTS

CSLD 2018 - ABSTRACTS

Characterization of Ocular Changes in Gaucher Disease

Cheryl Rockman-Greenberg[1] MD. MSc. PhD., Frank Stockl[1], Janine Johnston[1], Alie Johnston[1], Jeff Barnes[1], Leanne Zimmer[2], Aziz Mhanni[1], Don Duerksen[1], Michel Boutin[3] and Christiane Auray-Blais[3]
[1]University of Manitoba, Winnipeg, Manitoba, Canada; [2]Manitoba Association of Optometrists, Winnipeg, Manitoba, Canada; [3]Université de Sherbrooke, Sherbrooke, Quebec, Canada

Background: Gaucher disease (GD) is an autosomal recessive lysosomal storage disorder caused by *GBA1* mutations and resultant decreased activity of β-glucosidase. GD progression can occur despite treatment with enzyme replacement (ERT) or substrate reduction therapy (SRT). Progression is attributed to antibody formation, poor enzyme penetration, or GD natural history.

Case Study: Two siblings with GD type 3 and mild neurologic impairment on ERT and SRT were previously reported when severe protein-losing enteropathy and malabsorption 2^{o} calcified mesenteric lymphadenopathy developed in the younger sibling. His prior fundoscopic exams had been normal. Total parenteral nutrition including lipid was added to his treatment regime. Bilateral vitreous and pre-retinal deposits were identified when he presented 2 years later with a history of "floaters and orbs". Ocular findings progressed and visual acuity deteriorated requiring bilateral vitrectomies. Vitreous fluid was analysed for Glucosylceramide (GluCer) and Galactosylceramide (GalCer) isoforms by ultra-performance liquid chromatography – tandem mass spectrometry. His sibling has rare pinpoint white deposits adjacent to retinal vessels.

Results: A marked increase (>1252 times total) of 12 GluCer isoforms including two methylated isoforms was identified in our patient and was absent in the control sample. Residual deposits continue to clear now >1 year postoperatively with almost normal visual acuity.

Conclusions: This is the first documentation that the white vitreous and preretinal deposits seen in our patient and previously reported in GD 1 and 3 patients reflect the accumulation of GluCer substrate seen in GD. The origin of the GluCer is uncertain as is the reason for the discordance in expression from his affected sibling.

Acid Lipase Deficiency from Diagnosis to Therapy in Canada

Chitra Prasad[1,2,4], A. Dhandapani[1,2,4], S. Colaiacovo[1] and CA Rupar[1,2,3,4]
[1]Department of Paediatrics; [2]Children's Health Research Institute, London Health Sciences Centre; [3]Department of Pathology; [4]Western University, London, ON, Canada

Background: Lysosomal Acid Lipase (LAL-D) deficiency is an ultra-rare lysosomal storage disorder. Clinical features of late-onset form include dyslipidemia (elevated LDL, low HDL), elevated liver enzymes, hepatomegaly, and splenomegaly. This can progress to liver fibrosis and cirrhosis. LAL-D is caused by deficient activity of the LAL enzyme, resulting in the accumulation of cholesteryl esters and triglycerides throughout the body, predominately in the liver, spleen, gastrointestinal tract, and blood vessel walls. Supportive management with lipid-modifying agents, hematopoietic stem cell and liver transplant has been without major success.

Methods and Results: Over last 20 years we have had 3 patients with confirmed diagnosis of LAL-D. Two of the adult patients currently 31 and 40 years old presented with hepatosplenomegaly (The enzyme levels were at about 7% of control mean using fibroblasts and peripheral blood leukocytes). They are lost to follow up. 9 years old girl of French and welsh background presented with hepatomegaly, elevations in liver enzymes and dyslipidemia. LAL enzyme showed low levels of 13 pmol/hour (normal 80-230). She has c.684 delT and c.894 G>A pathogenic mutations.

Discussion: With the advent of Sebelipase Alfa Kanuma®, the 3rd patient has been started on intravenous Kanuma therapy every two weeks at 1 mg/kg. The therapy was started after significant advocacy from the family as the drug is not yet approved for coverage in Canada. She has tolerated the infusions well for last 21 months with no side effects. The liver enzymes and lipid profile have normalized. Clinical parameters are with in normal limits.

Pompe Disease: a New Approach for a Diagnosis in the Canadian Community

Fanny Thuriot[1] M.Sc., Marianne Doyon[1], Caroline Buote[1], Elaine Gravel[1], Elvy Lapointe[2], Pierre-Étienne Jacques[3,4], Karine Jacobs[5], Katherine Hodson[5], Serge Gravel[1] and Sébastien Lévesque[1]

[1]Department of Pediatrics, Université de Sherbrooke, Québec, Canada; [2]RNomique Platform, Université de Sherbrooke, Québec, Canada; [3]Department of Biology, Université de Sherbrooke, Quebec, Canada; [4]Department of Computer Sciences, Université de Sherbrooke, Quebec, Canada, [5]Dynacare, Laval, Quebec, Canada

Background: Late-onset Pompe disease (LOPD) is a rare autosomal recessive genetic disorder caused by alpha-glucosidase (GAA) enzyme deficiency leading to glycogen accumulation in lysosomes. Most patients develop respiratory insufficiency and progressive muscle weakness. Its resemblance with other muscle diseases and its rarity delays the diagnosis (on average 10 years post symptoms) and initiation of effective therapies.

Hypothesis: An early diagnosis may have benefic effects on the treatment. Screening of the GAA enzyme activity is performed when LOPD is suspected, but pseudodeficiency alleles may cause false-positive results. An alternative approach is gene sequencing.

Methods: We are in the process of testing 1500 patients from outpatient neurology clinics across Canada for a gene panel, including 94 genes associated with muscle disorders. Patients are recruited based on the presence of muscle weakness, unexplained respiratory insufficiency or symptoms supporting muscle involvement, in addition to the presence of laboratory evidence suggestive of muscle pathology: CK dosage, EMG, muscle biopsy or MRI. Dosage of the GAA enzyme activity is performed in parallel outside our institution.

Results: Of the 402 tested patients, we confirmed a diagnosis in 73 (18,2%), including 3 patients with LOPD. One pathogenic heterozygous variant in the GAA gene was identified in 6 patients and one variant of uncertain significance (VUS) was identified in 10 patients. Enzymatic activity correlated with the patients' carrier status.

Conclusions: Gene panel sequencing allowed the diagnosis of 18,2% patients with suspected muscle diseases in the Canadian community. LOPD accounted for 4,1% of all diagnoses.

Distribution of Heparan Sulfate and Dermatan Sulfate in Mucopolysaccharidosis type II Mice Tissues Using Tandem Mass Spectrometry

Iskren Menkovic B.Sc., Pamela Lavoie, Michel Boutin and Christiane Auray-Blais
Department of Pediatrics, Division of Medical Genetics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec

Background: Mucopolysaccharidosis type II (MPS II or Hunter Disease) is a multisystemic disease caused by a deficiency of the enzyme iduronate-2-sulfatase which impairs the glycosaminoglycan catabolism, more specifically heparan sulfate (HS) and dermatan sulfate (DS), leading to an accumulation in various organs and biological fluids. Enzyme replacement therapy (ERT) is provided to MPS II patients. To our knowledge, there are no studies allowing the individual and absolute quantification of HS and DS in tissues of affected MPS II mice compared to ERT treated, and control mice.

Hypothesis: There is a variability in the distribution of HS and DS in different organs and biological fluids in MPS II mice.

Method: Samples were homogenized, methanolized (55 min at 65°C), and resuspended in 90:10 ACN/H_2O with deuterated internal standards. Samples were filtered and 4 µL were injected onto a tandem mass spectrometer coupled to a liquid chromatograph (UPLC-MS/MS). A 6-minute method was adapted, optimized, and validated for HS and DS quantification in the brain, liver, small intestines, spleen, kidneys, lungs, urine and plasma for all mice groups.

Results: The validation of the UPLC-MS/MS method showed biases and relative standard deviation results at less than 12% for HS and DS in all matrices. Our results revealed a variability in the distribution of both molecules in different organs, with HS prominently increased, especially in the liver. Brain tissues showed an elevation in HS, while DS remained normal.

Conclusion: Ultimately, this research project will help improve our understanding of the physiopathology of the disease.

Pegunigalsidase Alfa - A Novel Enzyme Replacement Therapy for the Treatment of Fabry Disease: Preliminary Results from the Phase III Bridge Study

Micheal L. West M.D. BSc FRCPC FACP, D. Hughes, B. Vujkovac, C. Tøndel, K. Nicholls, A. Jovanovic , P. Giraldo, M. Langeveld, T. Hiwot E. Almon, S. Alon, B. Amit-Cohen, R. Chertkoff and A. Linhart

Dalhousie University, Department of Medicine, Division of Nephrology

Background: Pegunigalsidase-alfa is a novel PEGylated covalently-linked recombinant α-Galactosidase-A enzyme homodimer, for the treatment of Fabry disease (FD). Phase I/II studies in treatment naïve FD patients demonstrated that pegunigalsidase-alfa is efficacious, safe and well tolerated. Additionally, the data revealed pegunigalsidase-alfa's enhanced pharmacokinetics, with enzyme coverage throughout 2-week infusion intervals and reduced immunogenicity.

Methods: PB-102-F30 is an on-going Phase III, open label, switch-over study, assessing the safety and efficacy of pegunigalsidase-alfa in FD patients previously treated with agalsidase-alfa for at least 2 years which enrolls up to 22 adult patients, who switch from agalsidase-alfa to pegunigalsidase-alfa, 1mg/kg every other week for 12 months.

Results: Baseline characteristics of the first 14 patients (7 male, 7 female) enrolled: age range 27-60 y.o.; kidney function- 7/14 treated with ACEi or ARB, of which 3/14 presented proteinuria (978, 993, 2052 mg/gr); estimated glomerular filtration rate (eGFR) 69.87 and 86.03 mL/min/1.73m2 for males and females, with annualized eGFR slope of -10.8 and -5.1 mL/min/1.73m2/year, respectively; residual leukocyte enzymatic activity 5.8% and 27.9%, respectively and plasma lyso-Gb3 60.40 and 13.81 nM, respectively. Preliminary results of patients treated for at least 6 months with pegunigalsidase-alfa show improvement in the mean annualized eGFR slope, from -8.0 mL/min/1.73m2/year while on agalsidase-alfa, to +3.9 mL/min/1.73m2/year (from -10.8 to +1.1 in males and from -5.1 to +6.7 in females, respectively) after switching to pegunigalsidase-alfa.

Conclusion: The unique pegunigalsidase-alfa characteristics and these preliminary results further support the potential advantage of pegunigalsidase-alfa over the currently available FD therapies.

Urinary Galabiosylceramide (Ga_2): An Efficient Biomarker for Fabry Disease Patients with Residual Enzyme Activity

Michel Boutin Ph.D., Iskren Menkovic, Tristan Martineau, Vanessa Vaillancourt-Lavigueur, Amanda Toupin and Christiane Auray-Blais

Department of Pediatrics, Division of Medical Genetics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec

Background: Fabry Disease is an X-linked lysosomal storage disorder caused by the absence or decreased alpha-galactosidase A activity. This latter enzyme is involved in the recycling of cellular sphingolipids. Renal, cerebral, and cardiovascular manifestations of Fabry disease may result in premature death of patients. An untargeted metabolomic urine study by our group for untreated Fabry males and controls revealed 22 galabiosylceramide (Ga_2) isoforms/analogs as Fabry disease biomarkers. Unfortunately, the sensitivity (true positive/true positive+false negative) of these biomarkers was unsatisfactory for females and males having residual enzyme activity.

Hypothesis: The poor efficiency of Ga_2 as a Fabry disease biomarker for patients with residual enzyme activity results from the co-analysis of lactosylceramide (LacCer), a structural isomer of Ga_2

Method: A normal phase ultra-performance liquid chromatography-tandem mass spectrometry method was developed to separate 22 Ga_2 isoforms/analogs from their isobaric LacCer interferences. Urine samples from untreated Fabry males (n=34) and females (n=54), treated Fabry males (n=33) and females (n=19), and control males (n=34) and females (n=25) were analyzed.

Results: The chromatographic separation of Ga_2 from LacCer significantly increased its sensitivity especially for untreated Fabry females (from 9.3 to 70.4%).This study also highlighted significantly higher urinary levels of LacCer for females compared to males.

Discussion/Conclusions: In the context of personalized medicine, this novel analytical methodology will greatly improve the efficiency of Ga_2 as a Fabry disease biomarker for the diagnosis and monitoring of the disease. One untreated Fabry female presented a normal level of globotriaosylceramide (Gb_3), but had an abnormal level of Ga_2 in urine.

Ex Vivo Gene Therapy for Fabry Disease: A Phase 2 Clinical Trial

Shari Fallet, Chris Mason and **Nerissa C. Kreher MD, MBA, Chief Medical Officer, AVROBIO**
AVROBIO, Inc. & University College London

Background: *Ex vivo* gene therapy involves transplantation of genetically modified autologous stem cells to compensate for an underlying genetic defect. Lysosomal storage disorders (LSDs) are monogenic disorders that result from defective lysosomal function, leading to intra-lysosomal accumulation of non-metabolized macromolecules and subsequent cellular and organ dysfunction. Fabry disease is a LSD caused by mutations in the *GLA* gene that result in a functional deficiency of the enzyme, alpha-galactosidase A (AGA), which leads to pathological accumulation of glycosphingolipids throughout the body. Significant morbidity and early mortality result from damage to kidneys, heart, and brain.

Hypothesis: LSDs, including Fabry disease, are attractive candidates for *ex vivo* gene therapy based on the potential to transform a patient's own cells into a drug product that delivers functional protein after a single treatment.

Case Study/Methods: AVR-RD-01 is an *ex vivo*, lentiviral vector-mediated gene therapy being developed for the treatment of patients with Fabry disease.

Results: Results from a phase 1 safety trial in Canada have paved the path to the initiation of a Phase 2 clinical trial that will measure efficacy and safety in treatment-naïve males with classic Fabry disease. This phase 2 trial is multi-national and is currently approved in Australia and Canada and planned for United States and Japan. The first patient in this Phase 2 trial has been treated and early safety and efficacy results support continued clinical investigation of this approach for LSDs.

Discussion/Conclusions: Ex vivo gene therapy is an attractive and promising therapeutic approach for LSDs.

Monitoring of Patients with Morquio A Syndrome Using a Tandem Mass Spectrometry Analysis of Keratan Sulfate in Urine Specimens Collected on Filter Paper

Pamela Lavoie M.Sc., Christiane Auray-Blais LL.M., Ph.D
Department of Pediatrics, Division of Medical Genetics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec

Background: Morquio A syndrome is an autosomal recessive lysosomal storage disorder caused by a defect of the enzyme *N*-acetylgalactosamine-6-sulfatase, which plays a key role in the catabolism of keratan sulfate (KS), a glycosaminoglycan. Since 2014, enzyme replacement therapy (ERT) has been available for treatment of Morquio A syndrome. During clinical trials, urinary KS has been a useful biomarker and showed a marked decrease in patients on ERT, demonstrating therapy efficacy. Unfortunately, quantitative urinary KS testing is not widely available in biochemical genetics laboratories for efficient monitoring of treated patients.

Hypothesis: We hypothesized that a quantitative mass spectrometry KS assay using urine filter paper samples might be a solution to this issue.

Methods: The extraction of KS from the filter paper was performed using a NH_4OH 0.01M aqueous solution, followed by a 3-hour digestion at 40 °C with keratanase II. The detection of two KS-related disaccharides and creatinine was performed by tandem mass spectrometry.

Results: This validated methodology showed good intra-day and inter-day accuracy and precision (less than 11%). Urine specimens collected on filter paper were stable for at least 6 weeks. All Morquio A patients presented abnormal results pre-treatment compared to reference values.

Conclusions: Urine samples dried on filter paper facilitate the collection and shipping of samples to a reference laboratory by parents/patients, or healthcare practitioners for the analysis of KS. This approach involves a significant reduction of shipping costs and facilitates monitoring/follow-up of patients. It might also be applicable to high-risk screening in case of a clinical suspicion.

Transition from DMB Assay to an LC-MS/MS Method as First-Tier Test for Mucopolysaccharidoses: Experience of a Canadian Clinical Laboratory

Paula J Waters, Denis Cyr, John Mitchell, Bruno Maranda, Patrick Bherer

Division of Medical Genetics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec

Background: The DMB (dimethyl-methylene blue) assay of total glycosaminoglycans (GAG) is widely used in clinical laboratories, but is known to have significant limitations. LC-MS/MS methods allowing separation and quantification of individual GAG have recently been described. **Hypothesis:** Replacing the DMB assay in our laboratory by an LC-MS/MS method as first-tier test would improve diagnostic sensitivity, specificity and overall performance. **Methods:** We used a published LC-MS/MS method (H Zhang et al, Molec Genet Metab 114(2015):123-8), involving methanolysis and quantitation of dimers from heparan, dermatan and chondroitin sulfates. Over two years this assay was applied, in parallel with the DMB assay, to 50 samples from 19 known patients with MPS disorders, to 24 "blind" samples from external quality control schemes, and to over 200 samples received for routine testing. **Results:** Samples from 3 MPSIII patients showed normal DMB results but clearly elevated heparan sulfate by LC-MS/MS. In 20 samples from patients with MPS I, II, IVA or VI (most treated by enzyme replacement or bone marrow transplant), DMB results were normal but LC-MS/MS showed elevations of the relevant GAG species. In 27 samples from patients with various MPS disorders, both methods gave positive (abnormal) results, but the relative elevations above reference range were generally greater by the LC-MS/MS method. No samples from MPS patients gave abnormal DMB results but normal LC-MS/MS results. No false-positive results were obtained using LC-MS/MS, nor to our knowledge any false-negative results in untreated MPS patients. **Discussion/Conclusions:** The LC-MS/MS assay has now replaced the DMB assay in our laboratory, and undergoes long-term continuing evaluation of performance.

The Enzyme Replacement Therapy Vestronidase Alfa Stabilizes or Improves Disease Manifestations in Subjects with MPS VII <5-Years Old

Qais Abu Ali, MD[1]; Antonio Gonzalez-Meneses Lopez, MD[2]; David Viskochil, MD[3]; Pranoot Tanpaiboon, MD[4]; Esmeralda Martins, MD, PhD[5]; Shwetha Asha, MBBS[1]; Julie Taylor, PhD[1]; Tricia Cimms[1]; Chao-Yin Chen, PhD[1]; Christine Haller, MD[1]; Heather Lau, MD[6]

[1]Ultragenyx Pharmaceutical Inc, Novato, CA, USA; [2]Hospital Universitario Virgen del Rocío and Universidad de Sevilla, Seville, Spain; [3]University of Utah, Salt Lake City, UT, USA; [4]Children's National Health System, Washington DC, USA; [5]Centro Hospitalar Do Porto, Hospital de Santo António, Porto, Portugal; [6]NYU School of Medicine, New York, NY, USA

Background: Vestronidase alfa is an enzyme replacement therapy, approved in the US for the heterogeneous, ultra-rare, debilitating, lysosomal disorder Mucopolysaccharidosis (MPS) VII. **Hypothesis**: The open-label study CL203 (NCT02418455) is investigating the efficacy and safety of vestronidase alfa in subjects with MPS VII <5-years old. **Methods**: Eight subjects (age 1.7-5 years, mean weight 13.5kg) received vestronidase alfa 4mg/kg IV Q2W; 5 subjects completed treatment through Week 48 (W48).**Results**: Urinary glycosaminoglycans (uGAG) reduction from Baseline was sustained from W4 through W48 (LS mean [SE] of 64% [5%] at W4). Mean standing height increased from Baseline (86cm) to W48 (92cm); mean Z-score remained stable from Baseline (-2.27) to W48 (-2.12). Mean (SD) growth velocity (n=5) increased from 5.06 (1.89) within 2-yrs pre-treatment to 6.84 (1.58) cm/year at W48. Baseline hepatomegaly (n=3) and splenomegaly (n=2) resolved at W48 in 2 and 1 subjects, respectively. Clinical global impression scores improved or were unchanged. Two subjects had reliable Baseline and W48 functional development evaluations; both improved. Two subjects achieved all motor function evaluation milestones at W48 compared with 0 at Baseline. Six subjects developed anti-drug antibodies (ADAs); 2 had neutralizing antibodies, 1 had grade-1 anaphylactoid reactions during 2 consecutive infusions, managed with antihistamine. ADAs were not linked to reduced efficacy. No subject died or permanently discontinued therapy due to adverse events. **Discussion**: Vestronidase alfa-treated subjects with MPS VII <5-years old howed significantly reduced uGAG, stabilized or improved disease manifestations, and safety profile similar to older subjects. Possible growth improvement will be evaluated with continued treatment.

Podocyturia Evaluation for Fabry Patients Using a Tandem Mass Spectrometry Approach

Tristan Martineau[1] B.Sc., Michel Boutin[1], Anne-Marie Côté[1], Bruno Maranda[1], Daniel Bichet[2], Christiane Auray-Blais[1]

[1]Division of Medical Genetics, Department of Pediatrics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, QC, Canada; [2]Hôpital Sacré-Cœur, Université de Montréal

Background: Most analytical techniques for the assessment of podocyturia are tedious, time-consuming, and may lead to marked results variability. The aim of this research project was to devise an efficient analytical tool for the analysis of peptides of podocyturia using tandem mass spectrometry (MS/MS) for early diagnosis of various genetic and non-genetic kidney diseases.
Objectives: To develop and validate a simple and robust MS/MS method for the simultaneous analysis of podocin and podocalyxin using random urine samples, and to evaluate podocyturia in two specific groups of patients: those with Fabry disease and women with preeclampsia. Mass spectrometry control values were established.
Method: One mL of a random urine sample was treated and digested with trypsin (2 h at 37ºC). Tryptic peptides were purified by solid-phase extraction and evaporated. Samples were resuspended, filtered and analyzed using an Acquity ultra-performance liquid chromatography system coupled to a Xevo TQ-S MS/MS (Waters Corp.).
Results: Peptides ATFNPAQDK (*m/z* 496.3→558.3) and APAATVVDVDEVR (*m/z* 671.4→831.4) were selected for podocalyxin and podocin, respectively. Cleavable deuterated internal standards were synthesized for each peptide to correct matrix effects. Optimization of each analytical step was performed leading to a 10-minute chromatographic run with good peptide separation. Our results revealed statistically significant differences between podocalyxin levels in some Fabry patients and preeclampsia women compared to controls. Treated Fabry patients showed lower podocalyxin levels than untreated patients.
Conclusion: This MS/MS approach might offer a more reliable analytical tool for the evaluation of podocyturia in Fabry disease patients and preeclampsia women.

Describing Disease Burden Features of Treated Mucopolysaccharidosis Type 1 (MPS1) Population at the Hospital for Sick Children: A Retrospective Chart Review

Yaanu Jeyakumar BHSc, Michal Inbar-Feigenberg

The Hospital for Sick Children, Division of Clinical and Metabolic Genetics

Background: Mucopolysaccharidosis type I (MPS1) is a rare lysosomal storage disorder. Traditionally, MPS1 is classified as: Hurler (MPS1H), Hurler-Scheie and Scheie (MPS1A). Allogeneic hematopoietic stem cell transplantation (HSCT) is the current gold standard treatment for MPS1H. Enzyme replacement therapy (ERT) is the preferred treatment for MPS1A. The long-term clinical outcomes of HSCT and ERT vary considerably with a persisting residual disease burden reported.

Hypothesis/Objective: We aimed to describe parameters of disease burden for both patient groups treated in our facility over the past 15 years. We compared our findings with disease burden parameters reported in the literature.

Case Study/Methods: Retrospective chart review was conducted using data from all MPS1 patients, treated and followed at HSC between 2003 and 2018 (n=20).

Results: Of the 20 study patients, 14 were diagnosed with MPS1H and 6 with MPS1A. While 64% of MPS1H patients experienced decreased linear growth post-HSCT, the majority of MPS1A patients (83%) showed stable linear growth post-ERT. In both groups, mitral valve regurgitation and thickened valves were the most common cardiac findings. While thoracic spinal kyphosis and cord stenosis were the most frequent orthopedic manifestations in MPS1H, joint contractures were most common in MPS1A. Despite treatment, many clinical complications were found to either remain stable or progress. Neuropsychology assessments (MPS1H) revealed weakness in gross motor skills, fine motor skills, and attention. Two MPS1H patients were diagnosed with autism spectrum disorder.

Discussion/Conclusions: Many parameters are consistent with the reported literature. Autism as a possible complication post-HSCT should be further investigated.