ITALIAN JOURNAL OF PEDIATRICS

MEETING ABSTRACT Open Access

Lysosomal storage disorders for the pediatric rheumatologist: the example of mucopolysaccharydoses

Rolando Cimaz*, Angela Mauro

From 71st Congress of the Italian Society of Pediatrics. Joint National Meeting SIP, SIMGePeD, Study Group on Pediatric Ultrasound, SUP Study Group on Hypertension
Rome, Italy. 4-6 June 2015

The Mucopolysaccharidoses (MPS) are a group of diseases caused by complete or partial deficiency of lysosomal enzymes responsible for glycosaminoglycans catabolism. Their accumulation within the lysosome leads to cellular damage and organ failure [1,2].

The musculoskeletal system is the most frequently affected one. Joint stiffness, contractures (claw hand), dysostosis multiplex, and carpal tunnel syndrome are some of the most frequent features [3-9]. Often the joint symptoms may be confused with inflammatory arthritides such as Juvenile Idiopathic Arthritis [10,11]. A prompt differential diagnoses is a fundamental step: in MPS patients there are no signs of local inflammation such as swelling, warmth and tenderness, and lack of fever and increased inflammatory markers. In addition, patients with MPS do not respond to anti-rheumatic therapy [12,13].

In addition, characteristic facies, cognitive impairment, short stature, recurrent otitis media, sleep apnea, hearing, vision and heart problems can be present [14,15]. Because of a wide variety of clinical presentation, diagnosis of MPS disorders is often delayed, especially in patients with mild forms and without neurocognitive impairment such as Scheie Syndrome.

When clinical features are suggestive for MPS, the diagnosis is confirmed with the assay of urinary GAG concentration, which is a sensitive but not specific method [16] and, as the gold standard with determination of the specific enzyme in cultured fibroblasts, leukocytes, plasma or serum [17]. The genetic sequencing could be used to identify the disease-causing mutation.

The managment of MPS disorders requires a multidisciplinary evaluation for multi-organ involvement. The new therapeutic approaches to MPS have drastically changed the natural history of disease. Transplantation of hematopoietic stem cells from bone marrow or umbilical cord can achieve significant benefits. The clinical success of this therapeutic approach depends on age, stage of disease, type of donor and ability to achieve stable engraftment without the development of graft-vs-host disease [18,20]. In early stages of disease, enzyme replacement therapy can benefit musculoskeletal symptoms and lung function [21-23]. This therapy, however, does not cross the blood-brain barrier and has not shown neurocognitive benefit.

In conclusion, the goal is the prompt identification of MPS disorders since an early diagnosis could allow early treatment: in this regard, particular attention should be given to an accurate differential diagnosis with chronic inflammatory arthropathies.

Published: 30 September 2015

References

1. Muenzer J: **Overview of the mucopolysaccharidoses.** *Rheumatology (Oxford)* 2011, **50**:4-12.
2. Neufeld EU, Muenzer J: **The mucopolysaccharidoses.** In *The Metabolic and Molecular Bases of Inherited Disease.* New York: McGraw-Hill;Scriver CR 2001:3421-52.
3. Aldenhoven M, Sakkers RJ, Boelens J, de Koning TJ, Wulffraat NM: **Musculoskeletal manifestations of lysosomal storage disorders.** *Ann Rheum Dis* 2009, **68**:1659-65.
4. Schmidt H, Ullrich K, von Lengerke HJ, Kleine M, Brämswig J: **Radiological findings in patients with mucopolysaccharidosis I H/S (Hurler-Scheie syndrome).** *Pediatr Radiol* 1987, **17**:409-14.
5. Chen SJ, Li YW, Wang TR, Hsu JC: **Bony changes in common mucopolysaccharidoses.** *Zhonghua Min Guo Xiao Er Ke Yi Xue Hui Za Zhi* 1996, **37**:178-84.

* Correspondence: r.cimaz@meyer.it
Department of Pediatrics, Rheumatology Unit, AOU Meyer Hospital; Viale Pieraccini, n°24; 50139, Firenze, Italy

6. Montano AM, Tomatsu S, Gottesman GS, Smith M, Orii T: **International Morquio A Registry: clinical manifestations and natural course of Morquio A disease.** *J Inherit Metab Dis* 2007, **30**:165-74.
7. Mikles M, Stanton RP: **A review of Morquio syndrome.** *Am J Orthop* 1997, **26**:533-40.
8. Al-Qatan MM, Thomson HG, Clarke HM: **Carpal tunnel syndrome in children and adolescents with no history of trauma.** *J Hand Surg* 1996, **21B**:108-11.
9. Yuen A, Dowling G, Johnstone B, Kornberg A, Coombs C: **Carpal tunnel syndrome in children with mucopolysaccaridoses.** *J Child Neurol* 2007, **22**:260-3.
10. Morishita K, Petty RE: **Musculoskeletal manifestations of mucopolysaccharidoses.** *Rheumatology (Oxford)* 2011, **50**:19-25.
11. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, *et al*: **International League of Associations for Rheumatology classification of juvenile idiopathic arthritis. second revision Edmonton, 2001.** *J Rheumatol* 2004, **31**:390-2.
12. Cimaz R, Coppa GV, Kone-Paut I, Link B, Pastores GM, Elorduy MR, *et al*: **Joint contractures in the absence of inflammation may indicate mucopolysaccharidosis.** *Pediatr Rheumatol Online J* 2009, **7**:18.
13. Aldenhoven M, Sakkers RJ, Boelens J, de Koning TJ, Wulffraat NM: **Musculoskeletal manifestations of lysosomal storage disorders.** *Ann Rheum Dis* 2009, **68**:1659-65.
14. Vijay S, Wraith JE: **Clinical presentation and follow-up of patients with the attenuated phenotype of mucopolysaccharidosis type I.** *Acta Paediatr* 2005, **94**:872-7.
15. Thomas JA, Beck M, Clarke JT, Cox GF: **Childhood onset of Scheie syndrome, the attenuated form of mucopolysaccharidosis. I.** *J Inherit Metab Dis* 2010, **33**:421-7.
16. Mahalingam K, Janani S, Priya S, Elango EM, Sundari RM: **Diagnosis of mucopolysaccharidoses: how to avoid false positives and false negatives.** *Indian J Pediatr* 2004, **71**:29-32.
17. Hall CW, Liebaers I, Di Natale P, Neufeld EF: **Enzymatic diagnosis of the genetic mucopolysaccharide storage disorders.** *Methods Enzymol* 1978, **50**:439-56.
18. Weisstein JS, Delgado E, Steinbach LS, Hart K, Packman S: **Musculoskeletal manifestations of Hurler syndrome: long-term follow-up after bone marrow transplantation.** *J Pediatr Orthop* 2004, **24**:97-101.
19. Prasad VK, Kurtzberg J: **Transplant outcomes in mucopolysaccharidoses.** *Semin Hematol* 2010, **47**:59-69.
20. Boelens JJ, Wynn RF, O'Meara A, Veys P, Bertrand Y, Souillet G, *et al*: **Outcomes of hematopoietic stem cell transplantation for Hurler's syndrome in Europe: a risk factor analysis for graft failure.** *Bone Marrow Transplant* 2007, **40**:225-33.
21. McGill JJ, Inwood AC, Coman DJ, Lipke ML, de Lore D, Swiedler SJ, *et al*: **Enzyme replacement therapy for mucopolysaccharidosis VI from 8 weeks of age-a sibling control study.** *Clin Genet* 2010, **77**:492-8.
22. Schulze-Frenking G, Jones SA, Roberts J, Beck M, Wraith JE: **Effects of enzyme replacement therapy on growth in patients with mucopolysaccharidosis type II.** *J Inherit Metab Dis* 2011, **34**:203-8.
23. Wraith JE, Beck M, Lane R, van der Ploeg A, Shapiro E, Xue Y, *et al*: **Enzyme replacement therapy in patients who have mucopolysaccharidosis I and are younger than 5 years: results of a multinational study of recombinant human alpha-L-iduronidase (laronidase).** *Pediatrics* 2007, **120**:e37-46.

doi:10.1186/1824-7288-41-S2-A17
Cite this article as: Cimaz and Mauro: Lysosomal storage disorders for the pediatric rheumatologist: the example of mucopolysaccharydoses. *Italian Journal of Pediatrics* 2015 **41**(Suppl 2):A17.