Superimposed Mongolian spot and mucopolysaccharidosis VI

Erlane Marques Ribeiro[1]
Kalina Ribeiro Fontenele Bezerra[2]
Augusto César Cardoso-dos-Santos[3]
Charles Marques Lourenço[4]
Ana Elisa Kiszewski[5]

[1] Medical Genetics Service, Hospital Infantil Albert Sabin, Ceará, Fortaleza, Brazil
[2] Department of Dermatology, Federal University of Ceará, Fortaleza, Brazil
[3] Department of Genetics, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[4] Centro Universitario Estacio de Ribeirão Preto, Ribeirão Preto, São Paulo, Brazil
[5] Dermatology Service, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil

Address for correspondence:
Ana Elisa Kiszewski
Dermatology Service
Universidade Federal de Ciências da Saúde de Porto Alegre
Rua Sarmento Leite, 245, Porto Alegre, Rio Grande do Sul, BRAZIL CEP 90050-170
E-mail: kiszewski@gmail.com

Summary

Mucopolysaccharidoses (MPS) are a heterogeneous group of inborn errors of metabolism characterized by accumulation of glycosaminoglycans in several tissues. Extrasacral, extensive and persistent Mongolian spots (MS) were reported in some lysosomal storage disorders, mainly in MPS I, MPS II and MPS VI. The presence of superimposed MS has been very rarely reported. Here, we describe, for the first time, the association of superimposed MS in a patient with extensive and persistent MS and MPS VI.

KEY WORDS: mongolian spots; mucopolysaccharidosis; MPS VI.

Case synopsis

A 12-year-old Brazilian boy born to consanguineous parents. On physical examination he was noted to have skin phototype IV, extensive lesions present from birth as round and oval patches of blue-gray hyperpigmentation distributed over the back, shoulder, arms, legs, buttock and a small superimposed MS involving the sacrococcygeal area (Figure 1). There were only few features of MPS until 17 months of age when we evaluated the patient. He presented hepatosplenomegaly, stiff joint and dysostosis multiplex. MPS VI diagnosis was confirmed based on low arylsulfatase B (ARSB) activity in leukocytes, excessive urinary excretion of dermatan sulfate and identification of a homozygous mutation, IVS 5-8 T>G in *ARSB* gene. The patient has been receiving enzyme replacement therapy with N-acetylgalactosamine-4-sulphatase until 3 years old. He missed some programmed infusions. Despite improvement in certain aspects of the disease, follow-up showed slowly disease progression. MS had minimal regression (Figure 2). Physical abuse was excluded in this patient.

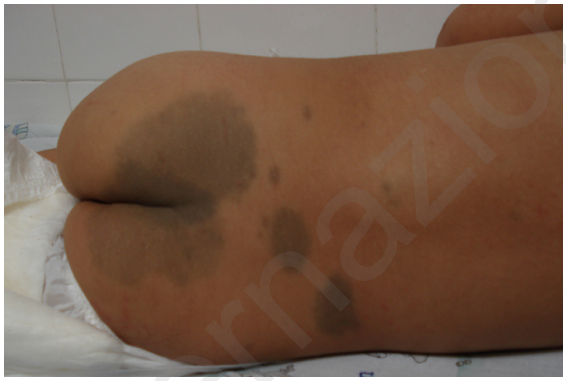

Figure 1 - At first evaluation with 17 months of age. Extensive round and oval patches of blue-gray hyperpigmentation present on buttocks and paraspinal area and a small superimposed MS involving the sacrococcygeal area.

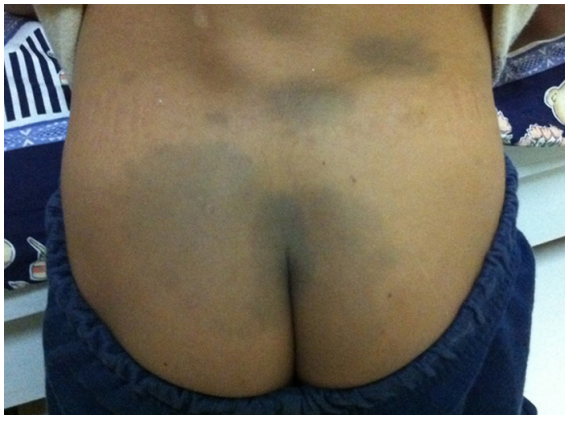

Figure 2 - Patient at 7 years of age with persistence of extensive Mongolian spot and superimposed spot.

Case discussion

Extensive and extrasacral Mongolian spots (MS) associated with inborn errors of metabolism (IEM) have been reported in literature (1-6). The association between mucopolysaccharidoses (MPS) and MS was described in MPS I (1, 2), MPS II (3, 4) and MPS VI (5, 6). The presence of superimposed MS has previously been very rarely reported in the literature only in healthy patients (7, 8). Although there is a cluster in Brazil, the incidence of MPS VI is 1:1.000.000 newborns (9, 10). To the best of our knowledge, the presence of superimposed MS in a patient with MPS VI has not been previously reported.

Mongolian spots are thought to be the result of failure of melanocytes to correctly migrate from the neural crest to the developing epidermis (7). Metabolic abnormality – such as accumulated heparan sulphate bound to tyrosine kinase type receptors – could prevent the natural process of development, maturation and regression of melanocytes in MS. Consequently, melanocytes may persist in dermis for a much longer period than in normal children (4, 6). The simultaneous presence of large light-grey patch and superimposed dark blue spot might be due to two different waves of melanocytic migration resulting in a different amount of dermal melanocytes in the two areas (8).

Mongolian spots at birth are large diffusely pigmented patch on the lumbosacral region, extending to both buttocks and the back, commonly observed in Japanese, African American and Hispanic infants. They usually affect healthy newborns and normally disappear as children grew older (2, 11). MS associated with IEM involves extensive areas of trunk and extremities and an increase in size and number over time without a reduction in its color (6). MS overlapped appears as a small darker pigmented MS superimposed on another MS and usually occur in children with extensive MS (7).

Although there are only two previously case reports in literature with MS and MPS VI (5, 6), Okamura et al. (2013) considered this condition would be common in MPS VI (5). Probably this condition is being underdiagnosed and this is because this sign has not been spontaneously reported by the families and physicians do not think about the association between MPS and MS.

Certainly, MS can be useful as clue to the diagnosis of IEM (6), but superimposed MS are so rare conditions that we do not know if superimposed MS and MPS VI are coincidental. Therefore, we suggest physicians should be alert to the possibility of a superimposed MS as new clinical sign of IEM.

Conclusion

We report the first case with extensive and superimposed MS and MPS VI in the same patient. This report reinforces the association of extensive MS with IEM.

Acknowledgements

We thank the subject reported in this paper as well as his family for their generous contributions.

Financial support

None.

Conflict of interest

Ribeiro EM and Lourenço CJ have received travel expenses for scientific meetings and speaker's honorarium from Biomarin. Bezerra KRF, Cardoso-dos-Santos AC and Kiszewski AE have no conflict of interest.

References

1. Ashrafi MR, Shabanian R, Mohammadi M, Kavusi S. Extensive Mongolian spots: a clinical sign merits special attention. Pediatr Neurol. 2006;34(2):143-145. doi:10.1016/j.pediatrneurol.2005.07.010.
2. Gupta D, Thappa DM. Mongolian spots: How important are they? World J Clin Cases. 2013;1(8):230. doi:10.12998/wjcc.v1.i8.230.
3. Ochiai T, Ito K, Okada T, Chin M, Shichino H, Mugishima H. Significance of extensive Mongolian spots in Hunter's syndrome. Br J Dermatol. 2003;148(6):1173-1178.
4. Ochiai T, Suzuki Y, Kato T, et al. Natural history of extensive Mongolian spots in mucopolysaccharidosis type II (Hunter syndrome): a survey among 52 Japanese patients. J Eur Acad Dermatol Venereol. 2007;21(8):1082-1085. doi:10.1111/j.1468-3083.2007.02203.x.
5. Okamura K, Munkhbat B, Batchimeg B, Tamiya G, Hozumi Y, Suzuki T. Case of a Mongolian child with extensive Mongolian spots in mucopolysaccharidosis type VI: identification of a novel mutation in the arylsulfatase B gene. J Dermatol. 2013;40(9):758-759. doi:10.1111/1346-8138.12237.
6. Ashrafi MR, Tavasoli A, Shiva S, Parvaneh N, Tamizifar B. Diffuse dermal melanocytosis in two patients with Sandhoff disease and mucopolysaccharidosis VI. Int J Dermatol. 2014;53(6):736-738. doi:10.1111/ijd.12303.
7. Leung AKC, Robson WLM. Superimposed Mongolian Spots. Pediatr Dermatol. 2008;25(2):233-235. doi:10.1111/j.1525-1470.2008.00641.x.
8. Musumeci ML, Lacarrubba F, Santagati C, Micali G. Multiple and superimposed Mongolian spots. Case Reports. 2013;2013(sep05 1):1-2. doi:10.1136/bcr-2013-200740.
9. El Dib RP, Pastores GM. A systematic review of new advances in the management of mucopolysaccharidosis VI (Maroteaux-Lamy syndrome): focus on galsulfase. Biologics. 2009;3:459-468.

10. Costa-Motta FM, Acosta AX, Abé-Sandes K, et al. Genetic studies in a cluster of Mucopolysaccharidosis Type VI patients in Northeast Brazil. Mol Genet Metab. 2011;104(4):603-607. doi:10.1016/j.ymgme.2011.09.017.
11. Gupta D, Thappa DM. Mongolian Spots-A Prospective Study. Pediatr Dermatol. 2013;30(6):683-688. doi:10.1111/pde.12191.