Journal of Inherited Metabolic Disease (2018) 41:1293–1294
https://doi.org/10.1007/s10545-018-0189-9

IMAGES IN METABOLIC MEDICINE

Severe ichthyosis in MPDU1-CDG

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Received: 20 February 2018 / Revised: 11 April 2018 / Accepted: 16 April 2018 / Published online: 2 May 2018

Abstract
Congenital disorders of glycosylation (CDG) have a broad spectrum of clinical manifestations. They can affect multiple organ systems, including skin and subcutaneous tissue. We report on an infant with severe ichthyosis caused by MPDU1 mutations. The case illustrates that skin manifestations are an important feature of CDG syndromes. Therefore, metabolic investigations should be included in the workup of infantile ichthyosis disorders.

Descriptive paragraph

Skin ichthyosis is a clinical feature of certain congenital disorders of glycosylation (CDG; e.g. SRD5A3-CDG, DOLK-CDG, PIGL-CDG). The pathogenic mechanisms causing skin abnormalities in CDG are still not fully understood. Theories include instability of key glycoproteins and/or accumulation of toxic sterol precursors (Rymen and Jaeken 2014).

Communicated by: Jaak Jaeken

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10545-018-0189-9) contains supplementary material, which is available to authorized users.

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The girl presented here is the third child of healthy consanguineous Turkish parents. An older brother suffered from an unclear neonatal-onset disease with facial dysmorphism, skin ichthyosis and cardiac malformations, including truncus arteriosus communis. He died during cardiac surgery in the neonatal period. The girl was born at 35 + 5 gestational weeks via caesarean section because of twin pregnancy. She showed muscular hypotonia, facial dysmorphism (hypertelorism, broad-based nose and thin lips), as well as a dry, squamous skin. Hands appeared small with scleroderma-like skin and loss of dermatoglyphic patterns. During the following months, the girl showed developmental delay and chronic feeding difficulties with failure to thrive. Microcephaly became evident. Skin ichthyosis worsened (see Fig. 1). Weight gain was inadequate and she showed recurrent episodes with diarrhoea. Moreover, she required constant oxygen therapy, suggesting a chronic lung disorder. Follow-up echocardiography at the age of 3 months revealed severe non-compaction cardiomyopathy (for the detailed case report, see the Supplementary Material).

Exome sequencing of the patient's DNA was performed as described previously (Kremer et al. 2016), which revealed a previously reported (Schenk et al. 2001) homozygous missense variant in *MPDU1* (NM_004870.3: c.[218G>A];[218G>A], p.[Gly73Glu];[Gly73Glu]), with both parents being heterozygous carriers. These findings were confirmed by Sanger sequencing. Isoelectric focusing of serum transferrin showed a type 1 pattern (increased a- and disialotransferrin; for further details, see the Supplementary Material).

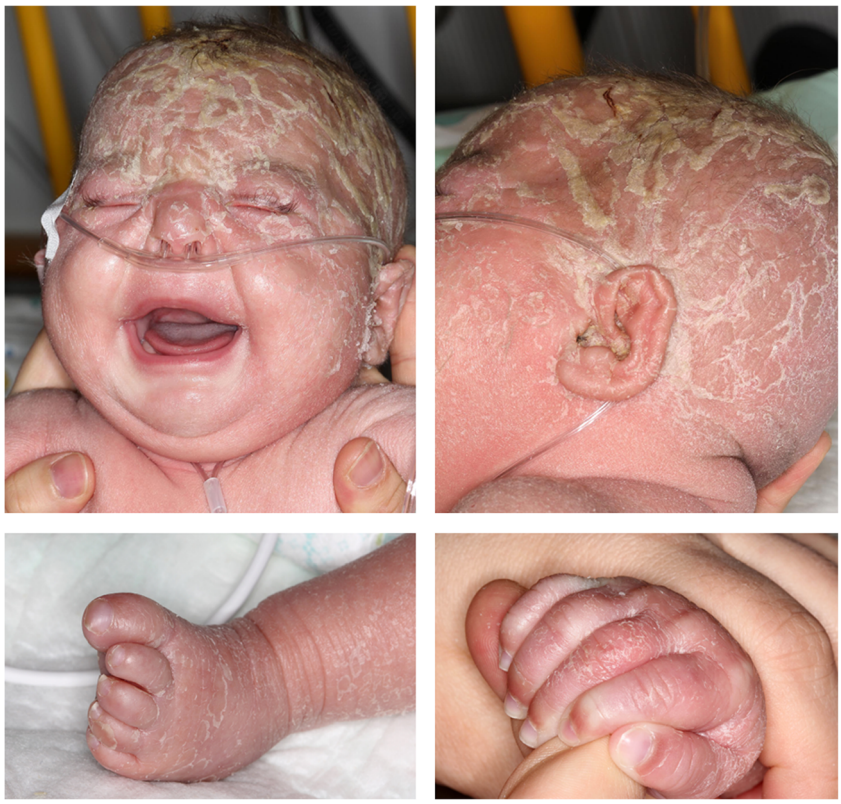

Fig. 1 Severe ichthyosis in a 3-month-old child with a pathogenic missense variant in *MPDU1*

Compliance with ethical standards

Conflict of interest C. Thiel, S. Wortmann, K. Riedhammer, B. Alhaddad, E. Mayatepek, H. Prokisch and F. Distelmaier declare that they have no conflict of interest.

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