Novel genotype of mevalonic aciduria with fatalities in premature siblings [case report]
Raupp, P.; Varady, E.; Duran, M.; Wanders, R.J.A.; Waterham, H.R.; Houten, S.M.

Published in:
Archives of disease in childhood

DOI:
10.1136/fn.89.1.F90

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Novel genotype of mevalonic aciduria with fatalities in premature siblings

P Raupp, E Varady, M Duran, R J A Wanders, H R Waterham and S M Houten

doi:10.1136/fn.89.1.F90

Updated information and services can be found at:
http://fn.bmj.com/cgi/content/full/89/1/F90

These include:

References
This article cites 4 articles, 2 of which can be accessed free at:
http://fn.bmj.com/cgi/content/full/89/1/F90#BIBL

Rapid responses
You can respond to this article at:
http://fn.bmj.com/cgi/eletter-submit/89/1/F90

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Topic collections
Articles on similar topics can be found in the following collections

- Genetics (3952 articles)
- Nutrition and Metabolism (1259 articles)
- Perinatal (1317 articles)

Notes

To order reprints of this article go to:
http://www.bmjjournals.com/cgi/reprintform

To subscribe to Archives of Disease in Childhood - Fetal and Neonatal Edition go to:
http://www.bmjjournals.com/subscriptions/
CASE REPORT

Novel genotype of mevalonic aciduria with fatalities in premature siblings

P Raupp, E Varady, M Duran, R J A Wanders, H R Waterham, S M Houten

Mevalonic aciduria is described in two very low birthweight siblings with unspecific clinical signs and recurrent septicemia. Both died within the first 2 months of life. DNA analysis showed a novel mutation in the gene encoding mevalonate kinase.

Mevalonic aciduria (MA; McKusick 251170) is a very rare inborn error of isoprene biosynthesis; so far only 20 cases have been reported, and six different disease-causing mutations identified. The earliest age at death of published cases of liveborn infants is 4.5 months.

CASE 1
A female infant (28 weeks gestation, 1100 g birth weight) was born to a consanguineous Arab couple who had a healthy son. Hepatosplenomegaly, raised levels of C reactive protein (53 mg/l), and thrombocytopenia (47 000/μl) were noted, but the initial blood and surface cultures and the differential white cell count did not suggest infection. Cytomegalovirus and Toxoplasma gondii IgM was negative. A blood culture taken on day 7 grew coagulase negative staphylococci. From day 12, while being treated with teicoplanin and amikacin, the patient deteriorated, with increasing abdominal distension, rising C reactive protein concentration, and radiological evidence of a low ileal obstruction. She was considered unfit for operation. She died on day 15 from multiorgan failure. Blood cultures taken during the neonatal period are scarce, and deaths within the first 4 months of life have not been published. In case 1, the parental consanguinity, congenital hepatosplenomegaly, and thrombocytopenia without definite evidence of infection made us consider an inborn error of metabolism. Although the clinical course in siblings has been claimed to be very similar, the hepatosplenomegaly, congenital hyperbilirubinaemia, and thrombocytopenia in case 2 were not congenital as in case 1, but developed later during septicemia and parenteral nutrition, as is commonly seen in very preterm infants. Intercurrent infections are known to trigger crises in MA. Apart from cataracts, cerebellar atrophy, skin rash, and dysmorphic features, which were not seen in our patients, hepatosplenomegaly, cholestatic liver disease, and thrombocytopenia have been associated with MA.

DISCUSSION
Data on the phenotype and laboratory indicators of MA mainly refer to long term observations, and emphasise the absence of hypoglycaemia, metabolic acidosis, or lactic acidemia. In affected families, prenatal diagnosis has been achieved, and stillbirths of malformed fetuses have been described. Reports on live births in whom MA was diagnosed during the neonatal period are scarce, and deaths within the first 4 months of life have not been published. In case 1, the parental consanguinity, congenital hepatosplenomegaly, and thrombocytopenia without definite evidence of infection made us consider an inborn error of metabolism. Although the clinical course in siblings has been claimed to be very similar, the hepatosplenomegaly, congenital hyperbilirubinaemia, and thrombocytopenia in case 2 were not congenital as in case 1, but developed later during septicemia and parenteral nutrition, as is commonly seen in very preterm infants. Intercurrent infections are known to trigger crises in MA. Apart from cataracts, cerebellar atrophy, skin rash, and dysmorphic features, which were not seen in our patients, hepatosplenomegaly, cholestatic liver disease, and thrombocytopenia have been associated with MA.
Owing to its rarity and unspecific symptoms, MA is probably underdiagnosed, especially in preterm infants who die early. The severity of the patient’s condition, parenteral nutrition, and prematurity do not interfere with the diagnosis of MA by determination of organic acids in urine. Our observation suggests that MA deserves to be considered in neonates who are born to consanguineous parents, and who suffer from recurrent life threatening infections or unexplained “sepsis-like” disease.

Authors’ affiliations
P Raupp, E Varady, Department of Paediatrics, Tawam Hospital, Al Ain, United Arab Emirates
M Duran, R J A Wanders, H R Waterham, S M Houten, Laboratory for Genetic Metabolic Diseases, Department of Pediatrics, Emma Children’s Hospital and Clinical Chemistry, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Correspondence to: Dr Raupp, Department of Paediatrics, Tawam Hospital, PO Box 15258, Al Ain, United Arab Emirates;
raupppeter@hotmail.com
Accepted 19 December 2002

REFERENCES

CORRECTION
The paper by Whitby et al (Low field strength magnetic resonance imaging of the neonatal brain Arch Dis Child Fetal Neonatal Ed 2003;88:F203–F208) was missing an acknowledgement. The authors wish to thank the “Babes in Arms” charity to whom they are extremely grateful for funding the work.