A new variant of galactose-1-phosphate-uridyltransferase (Gt Oron)

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INTRODUCTION

The enzyme galactose-1-P-uridyltransferase (Gt), which exhibits a genetic polymorphism, has an important function in the galactose metabolism. Its clinical importance is due to the fact, that the different gene products have different specific enzyme activities, which leads in the case of homozygosity for the null allele to galactosemia (Gt 0-0). Other forms with reduced activities, like the heterozygosity of the Duarte-variant with the null allele (Gt 2-0) are clinically significant as well (Schwarz et al, 1982). On the other hand, the Gt polymorphism has found routine application in forensic hemogenetics.

All newborns in Switzerland are routinely screened for galactosemia by analysis of dried capillary blood spotted on filter paper (Guthrie test) at day four of their life. The proband on whom we report here, has been identified in this screening. His Gt activity was markedly reduced.

MATERIAL AND METHODS

Newborn screening: Guthrie test samples were analyzed for Gt activity with the modified Beutler test (Scherz et al, 1972), and for free galactose by the semiquantitative method of Weidemann (1971).

Quantitative determination of enzyme activity was carried out by using ^{14}C-labelled gal-1P as a substrate (Stucki, 1982).

Phenotyping of Gt was done by electophoresis in agarose gel (Kühnl et al, 1974) and isoelectric focusing in agarose gel (Stucki, 1982).

Case description: The proband (E.D.), a normal newborn baby, was screened for galactosemia at day 6 of life. Reduced Gt activity was detected. The screening test was repeated at day 17 and at day 22, yielding the same result in both samples. Venous blood was then collected and we proceeded to the quantitative determination of the enzyme activity and phenotyping. A rare variant was detected and a family study was undertaken.

Advances in Forensic Haemogenetics 2
Edited by W. R. Mayr

RESULTS AND DISCUSSION

Phenotype patterns in agarose gel electrophoresis and isoelectric focusing are shown in figures 1 and 2 respecitvely. Enzyme activities are included in table 1.

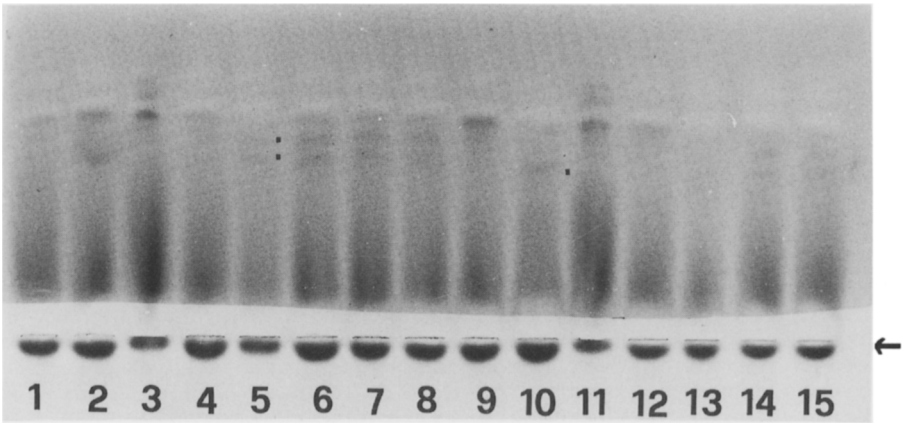
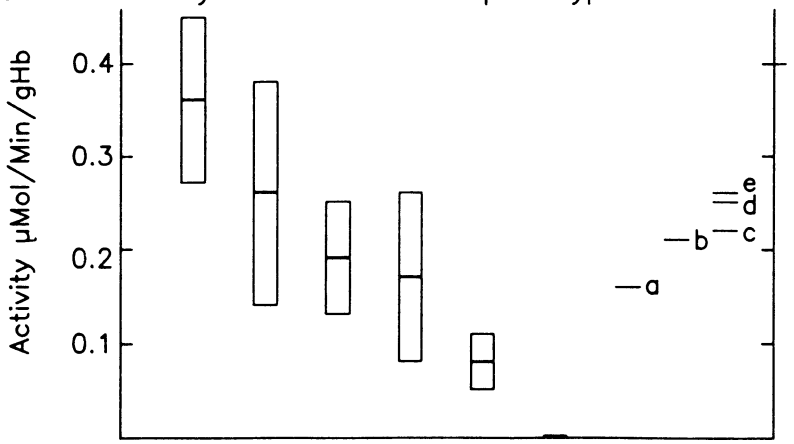


figure 1. agarose gel electorphoresis of galactose-1P-uridyltransferase.
Gt 1-1: 1, 2, 4, 9, 12; Gt 2-1: 3, 11; Gt Oron-1: 5, 6, 7, 8, 13, 14, 15;
proband (III/2): 5, 13; Gt Berne-1: 10
anode is at the top, origin is indicated by arrow

table 1 Activity of the different Gt phenotypes



a	proband	III/2	neonatal	0.158
b	proband		1 year	0.208
c	adult	II/4		0.218
d	adult	I/2		0.251
e	adult	II/2		0.262

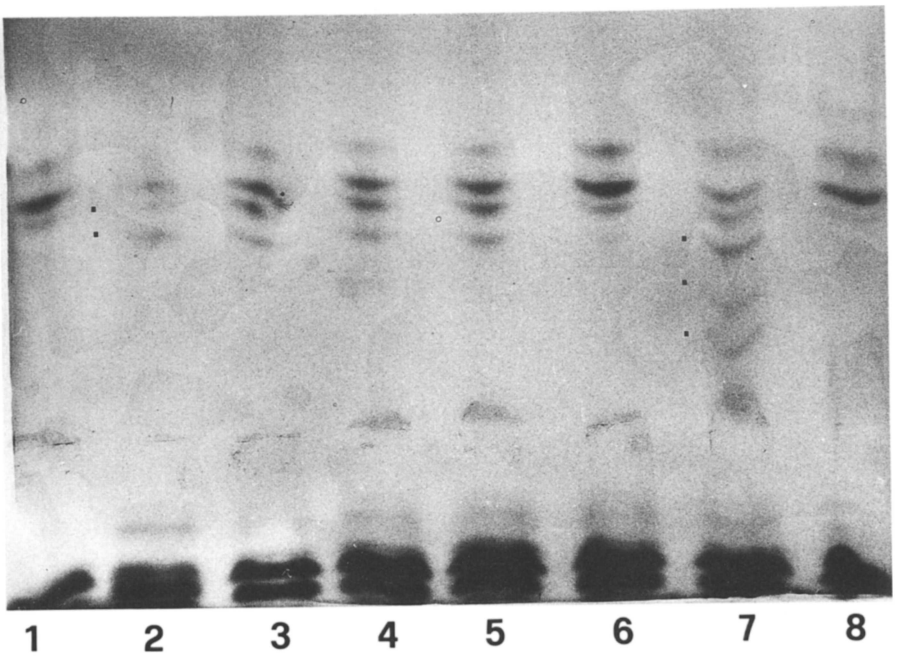
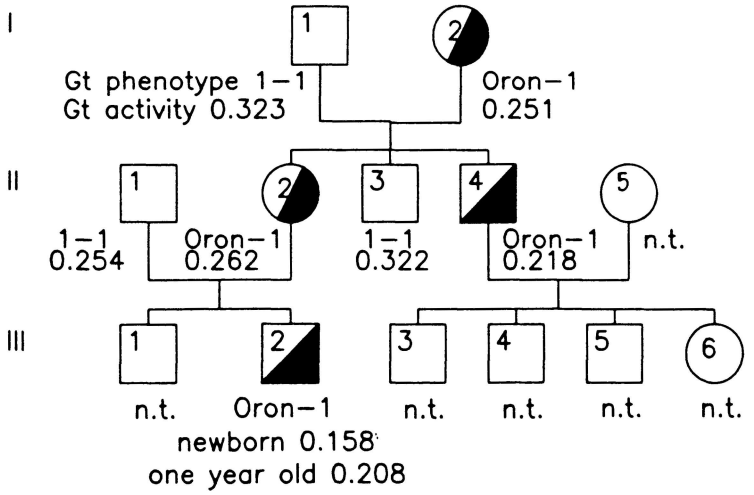


figure 2. isoelectric focusing in agarose gel
Gt 1-1: 1, 6; Gt 2-1: 8; Gt Oron-1: 2, 3, 4, 5;
proband (III/2): 2; Gt Berne-1: 7 anode is at the top

figure 3 Pedigree of family D.
proband = III/2



n.t. = not tested Activity in µMol/Min/gHb

The rare variant was present in heterozygous form with the common Gt 1 gene in all carriers of the family. The variant is slowly moving in electrophoresis compared to the Gt 1 bands. As it is shown in the pedigree of the family (Fig. 3), it was found in three generations.

Beside the two common Gt alleles (Gt 1, Gt 2), several rare ones are known (Negro, Rennes, Indiana, Los Angeles, Berne, Chicago I and II). Among them, only the Rennes, the Indiana, and the Berne variants are slowly migrating in electrophoresis compared to Gt 1. Figures 1 and 2 show, that the present variant is clearly different from the rare Berne variant we found earlier (Scherz et al, 1976). The other two variants (Rennes, Indiana) are no more available for direct comparison, but from their level of activity (6-10%, and 0-40% relative to Gt 1 respectively) (Baker et al, 1966, Schapira et al, 1969) it can be assumed, that they are different. We therefore considered our variant as "new", and we suggest to call it Gt Oron according to the place of residence of our proband. We observed an increase of activity of the erythrocyte enzyme during the first year of life of our proband. The adult carriers of the variant again had a slightly higher activity than the child. One can conclude form these activity levels, that the variant does not have clinical importance when it is present in the heterozygous form with the common type (Gt Oron-1). This assumption is supported by the fact, that the boy developed perfectly well with regular milk diet and that non of the adults who carry the variant reported on any problems of milk incompatability. In this respect, the situation looks similar to the one for the Duarte variant.

LITERATURE

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