Retrospective Diagnosis of GM1 Gangliosidosis by Use of a Newborn-Screening Card

To the Editor:

A deficiency of lysosomal β-D-galactosidase (βG; EC 3.2.1.23) is the primary defect in the three clinical forms (infantile, juvenile, and adult) of GM1 gangliosidosis and in Morquio B syndrome. Patients with the infantile form of GM1 gangliosidosis (type 1), who usually die before the age of 3 years, display the coarse face, hepatosplenomegaly, and skeletal dysplasia reminiscent of Hurler disease. Cases with later onset, described as the late infantile/juvenile form (type 2), display progressive psychomotor loss but less prominent dysmorphic changes. Extrapyramidal signs of protracted course are the major neurologic manifestations in the adult/chronic form (type 3) of GM1 gangliosidosis. Morquio B syndrome is expressed as generalized skeletal dysplasia with corneal clouding and normal intelligence *(1)*.

βG activity is also severely decreased in galactosialidosis, a disorder resulting from deficiency in cathepsin A/protective protein. This lysosomal protein forms a complex with βG and a second enzyme, neuraminidase (EC 3.2.1.18), at which point these enzymes are stabilized or protected from inappropriate lysosomal proteolysis. Affected individuals show a variable Hurler-like phenotype. Three phenotypic subtypes are recognized: the early infantile form, the late infantile type, and the most frequent, the juvenile/adult group. The demonstration of a combined deficiency of βG and neuraminidase in cultured skin fibroblasts is the preferred method of biochemical diagnosis *(2)*.

We present the first retrospective diagnosis of a GM1 gangliosidosis made with a dried blood spot from a newborn-screening card stored at room temperature for 15 months. The patient is a girl with an infantile type of GM1 gangliosidosis, diagnosed by clinical and standard biochemical procedures at 15 months of age. One dried blood spot from the newborn-screening card from the patient and one dried blood spot from each of three control cards sampled on the same date and stored in open plastic bags, also at room temperature, were sent to our laboratory in a blind way, identified by numbers. βG and β-hexosaminidase (EC 3.2.1.52), as a control enzyme, were measured (Chamoles NA, Blanco MB, Gaggioli D, Casentini C. Hurler-like phenotype: enzymatic diagnosis in dried blood spots on filter paper. Submitted for publication). The results of these assays are shown in Table 1. Although the activities of the enzymes may not be completely stable, a surprising amount of activity remained after 15 months. The βG activity in the patient card was <10% of that in the similarly stored control samples. Our laboratory has since introduced the assay of lysosomal enzymes in dried blood on filter paper *(3, 4)*. The newborn-screening card has been added to the biological materials that allow the identification of patients with GM1 gangliosidosis and probably of other lysosomal storage diseases, even after a long period of storage of cards at room temperature, when appropriate controls are used.

Table 1. Enzymatic activities in dried blood on filter paper.

		Activity, μmol · L⁻¹ · h⁻¹			
		βG		β-Hexosaminidase	
Samples	n	Range	Mean ± SD	Range	Mean ± SD
Healthy newborns	35	25.2–73.5	43.5 ± 13.3	554–1028	786 ± 165
Healthy adults	50	16.0–44.3	26.6 ± 7.3	335–803	532 ± 119
GM1G[a] patients	10	0–0.8	ND	626–1102	ND
GM1G carriers	10	3.9–9.8	ND	265–586	ND
MM, 7 days			2.3		726
Control 1			26.3		558
Control 2			29.0		584
Control 3			23.1		500
MM, 15 months			0.5		850
MM, father			14.6		393
MM, mother			10.2		447

[a] GM1G, GM1 gangliosidosis; ND, not done; MM, designation for patient.

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