Biochemical Study of Sialidosis Type I in a Russian Family

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A 7-year-old boy from a Russian family with decreased vision and a cherry-red spot but without any somatic and mental abnormalities is described in this paper. The decreased neuraminidase activity in the child's leukocytes and cultured skin fibroblasts and his 10-fold increase in urinary sialyloligosaccharides allowed us to conclude that he was affected by type I sialidosis. Some other results of the biochemical study of this child and his parents are presented. It is the first case of sialidosis in the Russian population.

The slowly progressing neurodegenerative diseases due to hereditary deficiency of neuraminidase have been described within recent years and classified as sialidoses (McKusick 25655). The occurrence of myoclonic convulsions, loss of visual acuity and a cherry-red spot in the maculae are characteristic clinical features of patients with sialidosis. Patients displaying at first only these symptoms of the disease are referred to as having type I sialidosis. Marked dysmorphic disturbances similar to those seen in Hurler disease, as well as in mental retardation, are observed in patients with type II sialidosis. Most patients found suffering from sialidosis have been Italians or Japanese (O'Brien, 1982). However, ethnic predilection for sialidosis is unlikely since single cases of sialidosis have been reported from other populations (Maire et al., 1981; King et al., 1984; Tsvetkova et al., 1984). The present report describes the biochemical features of sialidosis occurring in a boy from a Russian family, and the results obtained are compared with those reported by other authors.

CASE REPORT

The patient was a 7-year-old boy. He was born after a full term pregnancy from non-consanguineous parents of Russian descent. On routine physical examination at the age of six it was noticed that he had poor visual acuity and a cherry-red spot

MS received 24.1.86 Accepted 17.6.86
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in the macula. The boy had no somatic abnormalities and his mental development was normal. However, there were considerable changes in his electroencephalogram as compared to normal.

MATERIALS AND METHODS

Leukocytes, cultured skin fibroblasts and urine were studied. The activities of various acid hydrolases such as β-galactosidase, β-hexosaminidase and neuraminidase were measured using 4-methylumbelliferylglycosides (Koch–Light) by a method described earlier (Tsvetkova et al., 1979). The activities of arylsulphatase A and sphingomyelinase were measured with nitrocatecholsulphate and 2-hexadecanoyl-4-aminonitrophenyl-phosphorylcholine as substrates, respectively. The sialic acid content in leukocytes and fibroblasts was determined by the method of Warren (1959) after acid hydrolysis in 0.05 mol/L sulphuric acid at 80°C for 1 h. For the determination of urinary sialyloligosaccharides, urine samples were concentrated under vacuum evaporation and chromatographed by gel filtration on Sephadex G-15. The sialyloligosaccharide fractions were collected and assayed for sialic acid content using the resorcinol method of Svennerholm (1957). The sialyloligosaccharide patterns were examined by thin-layer chromatography on silicagel plates (Merck Kieselgel 60F254; propanol: concentrated ammonia solution: water 4:1:1 by volume). The amounts of free and total sialic acid in the urine were assayed before and after mild acid hydrolysis respectively, by our modified thiobarbituric acid method (Tsvetkova and Kozina, 1966).

Leukocytes were separated from whole blood using the dextran method (Scog and Beck, 1956). Fibroblasts were grown in Ham’s F-10 medium supplemented with 10% fetal calf serum. The cells were harvested by a mechanical procedure at the second–third passages. Leukocytes and fibroblasts were homogenized in distilled water and used for the estimation of enzyme activities and sialic acid content.

RESULTS

The activities of acid hydrolases such as β-galactosidase, total β-hexosaminidase, β-hexosaminidase A, arylsulphatase A and sphingomyelinase in the patient’s leukocytes were higher than control activities, except for β-galactosidase activity which was at the lowest control level (Table 1). The neuraminidase activity in the patient’s leukocytes was only one tenth of the mean control value. The neuraminidase activities in the leukocytes of the patient’s mother and father were reduced to heterozygote levels and constituted 37% and 57% of mean control activity respectively.

The additional data confirming the inherited deficiency of neuraminidase in this child were obtained in the study on neuraminidase stability upon freezing and thawing of leukocytes in liquid nitrogen. It is known that in sialidosis the labile fraction of the enzyme is absent (Suzuki et al., 1981). The neuraminidase activities before and after 5 cycles of freezing and thawing in liquid nitrogen were compared in the leukocytes of the patient and in those of a normal individual (Table 2). The

J. Inher. Metab. Dis. 10 (1987)