The Turkish Journal of Pediatrics 1996; 38: 85-89

GALACTOSIALIDOSIS IN TWO SIBLINGS*

*Aysel Yüce MD***, *Nurten Koçak MD****, *Guy T. Besley PhD*****

SUMMARY: Yüce A, Kocak N, Besley GT. (Gastroenterology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey, and Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, Manchester, United Kingdom). Galactosialidosis in two siblings. Turk J Pediatr 1986; 38: 85-89.

Galactosialidosis is a rare lysosomal storage disease associated with deficiencies of α-galactosidase and β-neurominidase. In this report, two siblings with galactosialidosis, resembling Niemann-Pick disease with the presence of foamy cells in multiple organs, splenomegaly and prominent hepatomegaly, are presented.

Galactosidase deficiency and an increased number of urinary sialic acid compounds were determined in these cases, and prenatal diagnosis was performed for their fourth sibling. Besides the presence of the typical clinical features, enzyme study is essential for the diagnosis of lysosomal storage disease and it facilitates in making the prenatal diagnosis.
Key words: lysosomal storage disease, galactosialidosis, α - galactosidase, β - neurominidase.

Galactosialidosis (GS) described by Goldberg et al.[1] is a lysosomal storage disease associated with decreased α-galactosidase and β-neurominidase activity due to lack of a protective protein. It is a well-established autosomal recessive disorder with several clinical types, such as early and late infantile and juvenile-adult forms, according to the age of onset and mortality. The symptoms include hepatosplenomegaly, severe edema, ascites during infancy, skeletal dysplasia, dysmorphism, ocular findings, neurological manifestations and mental retardation. The clinical diagnosis is supported by the presence of foamy cells in the bone marrow and multiple organs. But the definitive diagnosis requires urinary oligosaccharide chromatography followed by the appropriate enzyme studies[2-5].

Because of the rarity of this disease and the occurrence in four siblings, we report here in two siblings with GS diagnosed by enzyme studies. These cases appear to be the first cases reported from Turkey.

Case Reports

Case 1

A three-year-old girl was the first child of a first-degree consanguineous marriage. She was first seen with the complaints of abdominal distention and growth retardation. Her motor development was normal. On admission the physical

* From the Gastroenterology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, and Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital, Manchester.

** Associate Professor of Pediatrics, Hacettepe University Faculty of Medicine.

*** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

**** Top Grade Biochemist, Willink Biochemical Genetics Unit, Royal Manchester Children's Hospital.

examination revealed a well-looking child with a weight of 11 kg (< 5th percentile), a height of 89 cm (< 5th percentile) and head circumference 50 cm (75th percentile). She had mild mental retardation, coarse facial features, exophthalmic appearance, a short neck and depressed nasal bridge. Her liver was smooth and palpable eight cm and her spleen four cm below the costal margins respectively (Fig. 1).

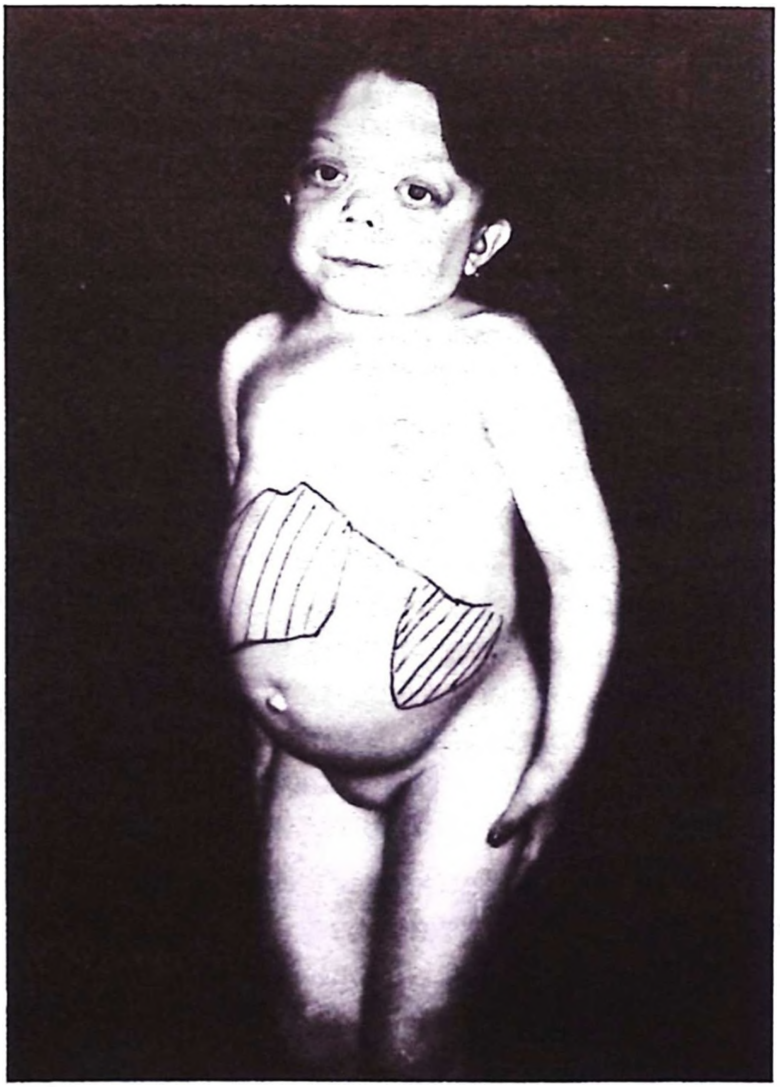

Fig. 1: The first case at 14 years of age. She had hepatosplenomegaly, coarse facial features, shot neck, macrocephaly and exophthalmic appearance.

The following laboratory data were within normal limits: complete blood counts, liver and renal function tests, serum triglyceride and cholesterol, urinary mucopolysaccharides, serum and urine amino acids and x-rays of the vertebrae. Bone marrow aspirate and liver biopsy disclosed foamy cells resembling those encountered in Niemann-Pick disease (Fig. 2). When the patient was admitted with pain in her right arm at nine years of age, a bone biopsy obtained from the right shoulder with a suspicion of osteomyelitis revealed the same type cells.

Sphingomyelinase activity in cultured skin fibroblasts and glucuronidase activity in leukocytes were normal. Leukocyte α-galactosidase was low (5% of control). In the urine, free sialic acid was 82.32 nmol/Omol Cr (control 20.4-37.1), and bound sialic acid was 281 nmol/Omol Cr (control 7.2-32.31). During follow-up the hepatosplenomegaly progressed, and palpebral edema and proteinuria were observed at the age of 13 years. Total serum proteins were 5.2 g/dl and albumin 2.6 g/dl. The patient died at home at the age of 15 years.

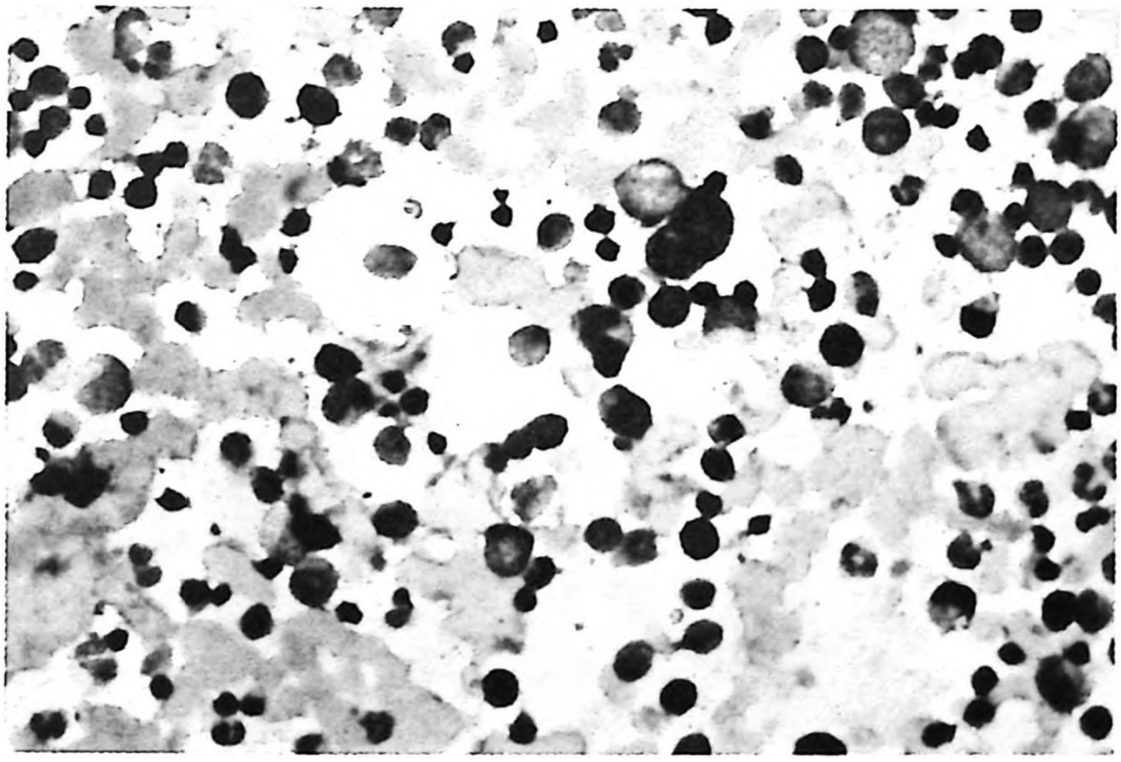

Fig. 2: Foamy cells resembling those seen in Niemann-Pick disease were present in the bone marrow.

Case 2

A three-year-old girl, the sister of the first case, was admitted to the hospital because of abdominal distention. Her weight was 13.5 kg (25^{th} - 50^{th} percentile). Her liver was smooth and palpable six cm and her spleen three cm below the costal margins, respectively. She had the same phenotype (Fig. 3) and laboratory findings of her elder sister. Sphingomyelinase and α-glucosidase activities were within normal limits. A deficiency of leukocyte α-galactosidase was found (5% of control). The urine contained increased amounts of free and bound sialic acids. During follow-up a 3/6 degree systolic murmur was heard along the left sternal border. Echocardiography indicated a thickening on the left mitral and aortic valves, as well as both mitral and aortic valve insufficiency. The patient is now 11 years old and has the same features.

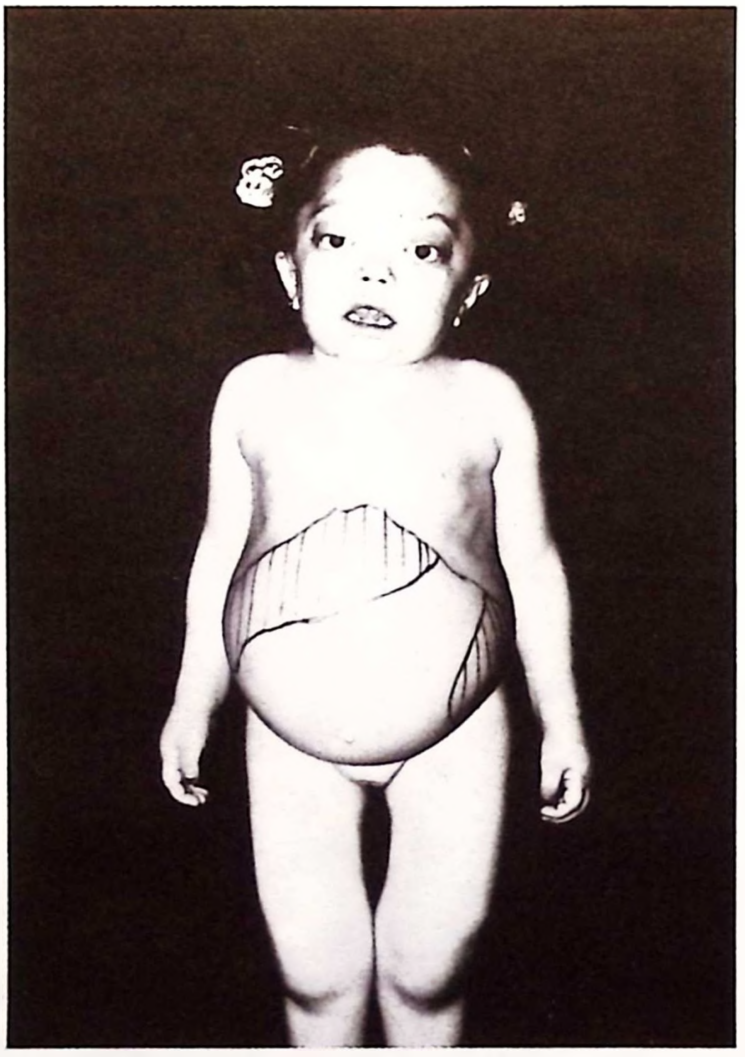

Fig. 3: Case 2 at 11 years of age. She presented with all the clinical features of galactosialidosis.

A third sister had died at two years of age following the development of abdominal distention, however no biochemical or necropsy studies had been done.

Prenatal diagnosis was performed for their fourth sibling. α-galactosidase and β-neurominidase deficiencies were found and the pregnancy was terminated[6].

Discussion

The clinical manifestations of GS result mainly from generalized sphingolipid storage and mimic GM_1 gangliosidosis. Foamy cells seen on bone marrow aspiration and multiple organs resemble Niemann-Pick disease[2].

The clinical presentations of our patients were suggestive of Niemann-Pick disease. But it was interesting that hepatomegaly in the two siblings was more

prominent than splenomegaly. The huge amounts of sialic acid compounds excreted in the urine as well as reduced α-galactosidase activity indicated that our cases belong biochemically to GS.

Miyashits et al.[7] classified this entity into three forms. The clinical features of the forms are highly heterogeneous, and intermediate forms are expected to be found. In fact these phenotypes may represent a continuous spectrum of phenotypes. Our patients appeared to fulfill some of the criteria of both late-infantile and adult forms of the disease.

Besides the classical features, endocardial and renal involvement are likely in GS[3, 8]. In the first case, proteinuria developed due to probable renal involvement. Unfortunately the renal findings could not be investigated. The second case had mitral and aortic insufficiency due to the cardiac component of the disease. Cardiac involvement, the most important clinical feature in management, has been reported in some cases of GS[8]. Patients with GS should be evaluated for both cardiac and renal findings. There is no effective therapy for GS; the management is based on clinical findings.

Studies on the molecular background of this autosomal recessive entity are continuing. The occurrence of the disease in all four children of this family is interesting, suggesting a different mode of inheritance. These cases also point to the importance of enzymatic assay in the diagnosis of lysosomal storage diseases. Enzymatic assay is also essential for accurate genetic counseling and facilitates in making a prenatal diagnosis in subsequent pregnancies.

REFERENCES

1. Goldberg MF, Cotlier E, Fichenscher LG, Kenyon K, Enat R, Borowsky SA. Macular cherry-red spot, corneal clouding and β-galactosidase deficiency: clinical, biochemical, and electron microscopic study of a new autosomal recessive storage disease Arch Intern Med 1971; 128: 387-397.
2. Okamura-Oho Y, Zhang S, Callahan JW. The biochemistry and clinical features of galactosialidosis. Biochem Biophy Acta 1994; 1225: 244-254.
3. Sewell AC, Pontz BF, Weitzel D, Humburg C. Clinical heterogeneity in infantile galactosialidosis. Eur J Pediatr 1987; 146: 528-531.
4. Usui T, Sawaguchi S, Abe H, Iwata K, Oyanagi K. Late-infantile type galactosialidosis. Arch Ophthalmol 1991; 109: 542-546.
5. Say B, Hommesa FA, Malik SA, Carpenter NJ. An infant with multiple congenital abnormalities and biochemical findings suggesting a variant of galactosialidosis. J Med Genet 1992; 29: 423-424.
6. Besley GTN, Cooper A, Thornley M, Sardharwalla IB, Koçak N, Yüce A. Prenatal diagnosis of galactosialidosis-an unexpected finding. Abstract Book of 29th SSIEM Annual Symposium, September 10-13, 1991, London, p. 79.
7. Miyashita K, Miyatani N, Yoshino H, Tsuji S, Miyatake T. Late-infantile form galactosialidosis with psychomotor retardation and spastic paraparesis. Clin Neurol 1989; 29: 1244-1250.
8. Rosenberg H, Frewen TC, LI MD, et al. Cardiac involvement in diseases characterized by β-galactosidase deficiency. J Pediatr 1985; 106: 78-80.