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HYPERAMMONEMIA ASSOCIATED WITH GLYCOGEN STORAGE DISEASE TYPE I*

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Neonatal hyperammonemia leads to overwhelming and potentially fatal illness. Most reports of patients in whom hyperammonemia occurred in the immediate newborn period stress the grave prognosis of this condition [1,2].

Hyperammonemia develops primarily as a consequence of an inherited defect in one of the enzymes of the Krebs-Henseleit cycle of urea synthesis [1-5]. Other metabolic defects that may be present with symptomatic hyperammonemia include organic acidemias [6,7], defects in lysine metabolism [8,9] and the familial syndrome of hyperammonemia, hyperornithinemia and homocitrullinuria [10-12]. Further causes and conditions associated with hyperammonemia include hepatic failure [13], congestive heart failure [14], erythroblastosis fetalis [15], parenteral alimentation [16], pulmonary hemorrhage [17], transient hyperammonemia of the preterm infant [18] and recently, perinatal asphyxia [19].

This report describes a new cause of secondary hyperammonemia associated with glycogen storage disease type I. To our knowledge, there is no report in the literature describing the coexistence of glycogen storage disease and hyperammonemia.

Case Report

F.A., a 3250 gm male infant was born at 40 weeks gestation to a 24-year-old multigravida woman after an uneventful pregnancy and delivery. In the second day of life he developed seizures, and irregular eye movements were noted. Because of these findings he was admitted to the Neonatology Unit, Hacettepe University Institute of

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Child Health. Family history revealed that the parents were first cousins and that two of the infant's brothers had died at 3 days and two and one-half months of life, respectively.

On physical examination the patient appeared tachypneic, and the liver was palpable 6 cm below the right costal margin. He had hypertonicity and lacked the usual newborn reflexes. Other system findings were unremarkable.

Laboratory studies including a complete blood count, urinalysis, blood electrolytes, cultures, cerebrospinal fluid examination and repeated blood and urine amino acids and organic acid analyses were all normal. Remarkable laboratory findings were hypoglycemia, hyperuricemia, lactic acidemia, acidosis and hyperammonemia (369.2 μg/dl) (Table I). The daily course of blood ammonia is shown in Figure 1. An exchange transfusion was performed for hyperammonemia and acidosis on the fifth day of life, and a protein-free diet was started.

The infant also underwent liver biopsy which revealed swelling in the hepatocytes, vacuolar degeneration and moderate fatty infiltration. Glycogen content of the liver tissue was 30 gm per 100 gm of tissue (normal up to 5 gm per 100 gm liver tissue).

On the 24th day of life the infant developed gastroenteritis. Stool culture yielded enteropathogenic E.coli. Despite appropriate therapy for gastroenteritis with intravenous fluid, he developed sepsis and died on the 28th day of life.

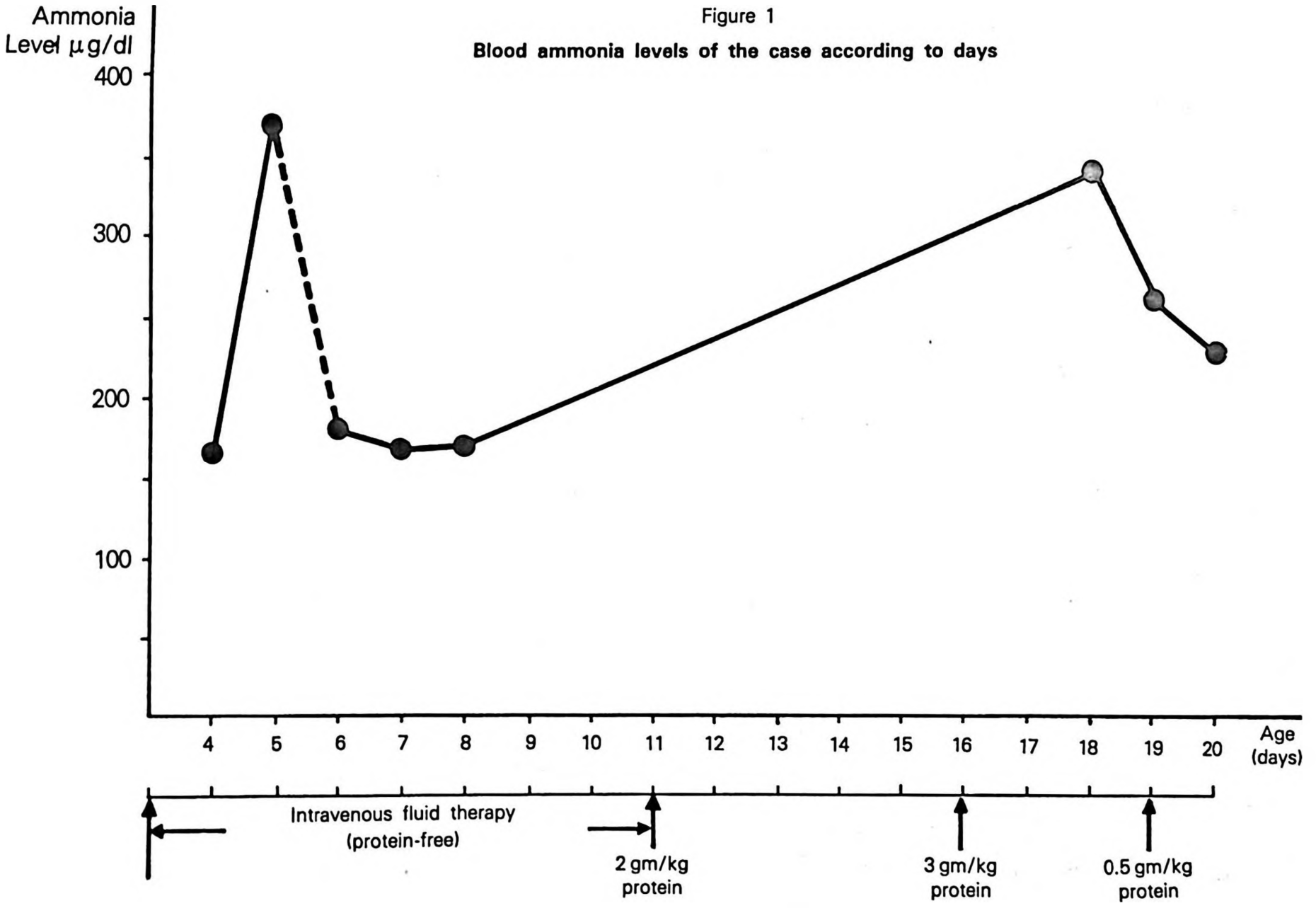
TABLE I

Laboratory Findings

Age (days)	Blood glucose mg/dl	Lactic acid mg/dl	Ammonia level μg/dl	Blood urea nitrogen mg/dl	Uric acid mg/dl	Blood pH
3	0					
4	11		164.4			7.35
5	11	42	369.2			7.11
6	200		183.3			
7	29		170	70	17.2	
8	140	52	173	50	8.2	
11	29					
13	29					
14	19					
15	23					
18	47		342.8	45	6.	
19	41	92	261.5			7.17
20	76		230			7.19

Figure 1

Blood ammonia levels of the case according to days



Discussion

Major clinical and laboratory features of glycogen storage disease type I are hepatomegaly, hypoglycemia, lactic acidemia and hyperuricemia[20-23]. All these features were also found in our case (Table I). A definitive diagnosis of glycogen storage disease is made by measuring the amount of glycogen or showing changes in the molecular structure of tissues[20], and to this end the infant underwent liver biopsy, the pathological and biochemical findings of which confirmed glycogen storage disease, an inherited autosomal recessive disease. All these findings, along with family history of early death in siblings strongly suggested glycogen storage disease type I in our patient.

There is no previous report describing hyperammonemia in glycogen storage disease. Hommes et al[24] reported hyperammonemia in an infant with carbohydrate metabolism changes who had carbamyl phosphate synthetase I deficiency. In this case there was hyperglycemia and decreased levels of blood pyruvate and lactate. There was also decreased hexokinase activity, and glucokinase was found in the liver. The authors postulated that urea cycle activity changes may have been the cause of alterations in carbohydrate metabolism.

Hyperammonemia was a prominent finding in our case. Elevated levels persisted during protein-free feeding (Figure 1) and despite exchange transfusion. All attempts to determine the cause of hyperammonemia, including amino acid and organic acid analysis, were unsuccessful.

Inhibition of multiple enzyme reactions in acidosis and lactic acidemia has been reported[25]. Hyperammonemia may have developed due to such an inhibition of enzyme reaction in our case also. The observation of hyperammonemia in this case suggests that this finding should be considered as a possible contributing factor to the clinical signs of glycogen storage disease.

Summary

Hyperammonemia associated with glycogen storage disease type I is described as a new observation in neonatal secondary hyperammonemias, and the possible contributing effect of hyperammonemia to the clinical signs of glycogen storage disease type I is emphasized.

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