A Case Associated with Abdominal Ascites Accumulation in Congenital Disorder of Glycosylation Type Ia

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Introduction

Congenital disorders of glycosylation (CDG) are a rapidly expanding, clinically and genetically heterogenous group of diseases caused by different abnormalities in the glycan synthesis pathways. CDGs affect multiple organs including the brain, eyes, musculoskeletal, liver, and hematologic systems. Hepatopathy has been described in various CDG including phosphomannomutase deficiency (PMM2-CDG), the most commonly identified CDG, MPI (phosphomannose-isomerase), ALG8 (glucosyltransferase II), ALG1 (mannosyltransferase I) and COG (conserved oligomeric Golgi complex) deficiencies. The incidence/prevalence of all types of CDG haven't been just determined. CDG is classified CDG-I and CDG-II. CDG-Ia of these is more common and affected children have a 25% mortality rate.

Case

At 12 months, he was admitted for distended abdomen further progressed and referred to our department for complex evaluation and assessment. At this time, we observed a notable psychomotor retardation, significant central hypotonia, limited spontaneous movement, poor eye contact, no reaction on noise, significant failure to thrive. He was second child of healthy unrelated parents.

The boy was delivered at term after an uneventful pregnancy. The family history was unremarkable. His weight was 6kg(3th P), length 68cm(3th P) and head-circumference 42cm(<3th P). He had prominent ears, triangular face, micrognathia, inverted nipples, abnormal fat distribution over his thighs, buttocks and suprapubic regions and a large Mongolian spot in his gluteal region. He was distended abdomen and then subsequently developed a predominantly ascites and hepatosplenomegaly (Figure 1). Laboratory evaluation revealed ALT: 116U/L(0-41), AST: 376U/L(0-40), GGT: 41U/L(0-60) glucose: 53mg/dl(70-110), albumin: 2.8gr/dl(3.5-5), protein in urinalysis: 300mg/dl(0-25). Liver biopsy was interpreted as pre-cirrhotic/cirrhotic. Cranial Magnetic Resonance Imaging revealed cerebral/cerebellar atrophy (Figure 2). During follow-up, the patient had a clonic seizure and pleural/pericardial effusion secondary to infection. Clinical symptoms and laboratory findings led to the strong suspicion of CDG. Screening for CDG performed by the use of isoelectric focusing of serum transferrin showed pronounced increases in disialotransferrin and asialotransferin with a corresponding reduction in tetrasialotransferrin. This pattern supports the diagnosis of PMM2-CDG. To further confirm the genetic cause of the disease exome sequencing was performed. A compound heterozygous pathogenic mutation was detected (c.385G>A/ c.422G>A) in *PMM2* gene. He was diagnosed with CDG-type1a. His healthy parents were carriers for these variants.

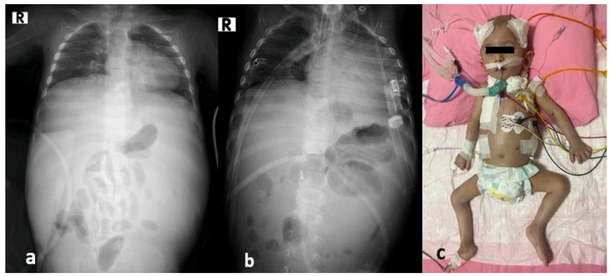

Figure 1. a-Postero-anterior lung(PA) radiography at first admission, b-PA radiography (subsequent application), c-Photograph of the patient

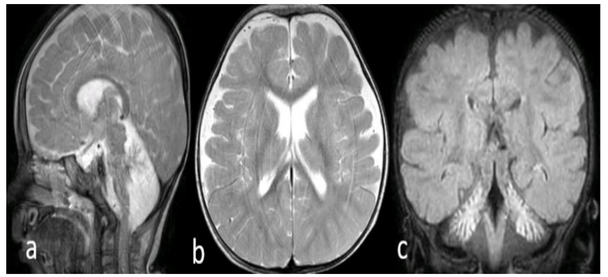

Figure 2. Cranial Magnetic Resonance Imaging (a-sagittal T2, b-axial T2, c-coronal)

Discussion

CDG-Ia is a rare autosomal recessive genetic disease caused by mutations in the phosphomannomutase 2 (*PMM2*) gene. It often presents multiple systemic symptoms, including developmental delay, hypotonia, hepatopathy, coagulopathy, inverted nipples, uneven distribution of subcutaneous fat, and feeding difficulties. In addition cases with ascites, pleural/pericardial effusion have been reported and is estimated to occur in 30% of the patients with CDG type Ia. A small percentage of the patients with CDG type Ia may be borned with intra-uterine hydrops fetalis, which is a lethal condition. Analysis of carbohydrate-deficient transferrin and protein-bound glycans by mass spectrometry can diagnose CDG subtypes. Genomic sequencing is needed for definite diagnosis.

Conclusions

There is no curative therapy for the PMM2-CDG at the moment, but other supportive care options were available to be offered. The definite diagnosis of PMM2-CDG can also assist in the process of genetic counseling, family planning, and preimplantation genetic diagnosis. We wanted to emphasize the importance of keeping in mind the broad phenotypic/genetic etiology of CDG in patients presenting with multisystem findings such as developmental delay, liver involvement.

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