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Case Report

An infant with trichohepato-enteric syndrome: case report

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ABSTRACT

Trichohepato-enteric syndrome (THE-S) is a disease characterized by severe infantile diarrhea, failure to thrive, facial dysmorphism, woolly hair, and immune or hepatic dysfunction. We report the case of a boy who presented in early infancy with chronic watery diarrhea, dependent on total parenteral nutrition, along with other features of THE-S.

Keywords: Intractable diarrhea, Infant, THE-S

INTRODUCTION

Several case reports have discussed trichohepato-enteric syndrome (THE-S), an autosomal recessive disease with prevalence of 1:1,000,000. A rare genetic disorder caused by mutation in SKIV2L or in TTC37.[1] The reviewed literature showed 9 clinical signs are associated with THE-S.[1] There are 3 signs that are always present: intractable diarrhea, facial dysmorphism and hair abnormality. In more than 90% of cases, patients have IUGR and immunodeficiency; other less frequent manifestations include: skin abnormalities, liver disease, congenital cardiac defects and platelet abnormalities.

CASE REPORT

This is the case of a 21 month old male patient, born full term, by Cesarean section due to cephalo-pelvic disproportion to G4P3A1L3D1 mother with a third degree consanguinity between parent. The course of pregnancy was smooth, his birth weight was 3500 gram. There was no significant family history. He presented with a history of chronic watery diarrhea since the first week of life. He was hospitalized many times with no evident diagnosis. Patient was maintained on IV fluid and total parentral nutrition, with mild improvement due to bowel rest. Patient was maintained on breast feeding after birth then changed to several specialized formula (protein hydrolysate, amino acid based formulas, and glucose galactose free formula) but diarrhea persisted with a frequency more than 20 episodes per day. During his hospitalization he developed bacteremia and several episodes of chest infections.

Upon presentation patient's weight was 5 000 gm (less than 5th percentile), his length, and occipito frontal circumference were below the 5thpercentile. Patient was pale, hypoactive, dehydrated with prominent forehead, sunken eyes, depressed nasal bridge, thin brittle hair, severe muscle wasting, patient had a distended abdomen with hepatosplenomegaly and petechae over the chest and abdomen along with global developmental delay (Figure 1).

Initial investigations revealed hemoglobin 8g/dl, WBC 10,000 (neutrophils 40%, lymphocytes 51%, monocytes 6%), platelets 60,000, albumin 2 g/dl, electrolyte disturbances with hypokalemia and metabolic acidosis (HCO3 9 meq/dl) and mildly elevated liver function tests (SGPT :70 U/L, normal = 0-50U/L).

Several investigations were done including: Immunoglobulins levels and flow cytometry were normal. Urine, stool and blood cultures showed no growth. Stool for reducing substances and sudan stain were negative, IgE specific for cow milk, antiendomysial, antitranglutaminase antibodies were negative. Plasma amino acids, urine organic acids were normal. Bone marrow aspirate showed hypercellular bone marrow; gastroscopy and jejunal biopsy were done, pathology revealed relatively short and broadened surface villi (although that the patient was put on gluten free diet, diarrhea didn't improve). Patient was maintained on total parenteral nutrition for more than 6 months along with IV fluid. Despite that he still had diarrhea but with less frequency, and he was discharged on a glucose galactose formula,oral rehydration solution and PO sodium bicarbonate. Based on the facial features associated with the chronic diarrhea with no identified cause, the patient was diagnosed with Tricho-hepato-enteric Syndrome.

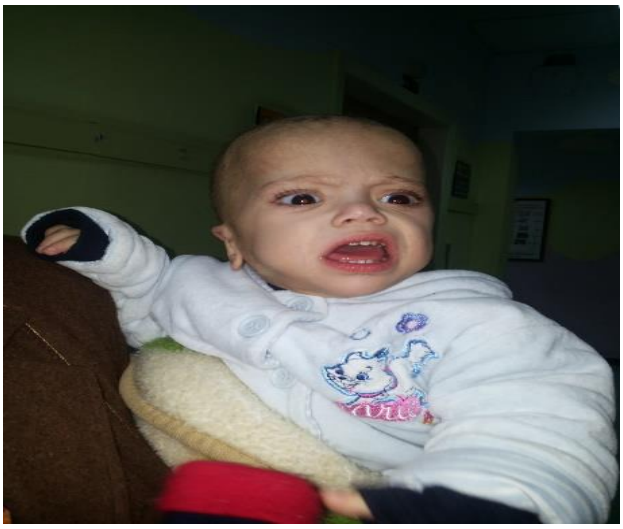

Figure 1: Facial dysmorphism.

DISCUSSION

The patient has many features that are similar to THE-S, which include facial dimorphisms, intractable diarrhea, hair abnormality, failure to thrive, and hepatic involvement. The onset of diarrhea was in the first week of life, the patient was extensively investigated. Histological exam of intestinal biopsy failed to find any explanation for the diarrhea in the patient.

THE-S is caused by a mutation in either TTC37 (60 %) or SKIV2L (40 %), it is an autosomal recessive disease, a rare and severe bowel disorder that involve two genes encoding subunits of the SKI complex. The estimated prevalence is 1/1,000,000 births.[1]

44 cases have been published between 1982 and 2012. Literature reviewed showed that 9 clinical signs are associated with THE-S.[2-15] Three are constant: intractable diarrhea, facial dysmorphism and hair abnormality. Two are very frequent (more than 90%): IUGR and immunodeficiency; 2 are frequent: skin abnormalities and liver disease and 2 are rare: congenital cardiac defects and platelet anomaly.[1-14]

The phenotypic presentation of THE-S is heterogeneous, and ranges from mild to severe form, which is characterized with long-term parenteral nutrition, and in some patients, typically it lasts for months to years, to achieve adequate nutrition and growth.[12] However, long-term parenteral nutrition should not be started in patients with concomitant liver disease. In case with abnormal antibody production, immunoglobulin administration may be required.[1] Patients with THE-S are also at increase risk of developmental delay, therefore early neurorehabilitative therapy should be started once developmental delay is identified.

The challenge in diagnosing of THE-S originates from the clinical heterogeneity of the disease, the prognosis of THE-S has improved withyears, but the mortality rate is still high. The maincomplications are liver disease and infections.[15] Some patients are weaned off parenteral nutrition butothers remain under parenteral dependence for morethan 10 years.[15]

Finally THE-S is the first mendelian disease related to cytoplasmic exosome anomaly, and at least 2 genes are involved, it is a genetic disease that could be suspected in cases of intractable diarrhea with hair abnormalities.

The genetic test that was done and the mutations in TTC37 or SKIV2L were not detected.

Despite that we found three case reports that showed no mutations in latter genes as well 2, where each case showed different gene mutations. So our diagnosis was made on clinical basis.

Although recently improvements have been made regarding molecular study and diagnosis, the prognosis remain the same.

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