case report

Mitochondrial Neurogastrointestinal Encephalomyopathy Treated with Stem Cell Transplantation: A Case Report and Review of Literature

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Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessive disorder. The mutation in the ECGF1 gene causes severe deficiency of thymidine phosphorylase (TP), which in turn increases thymidine and deoxyuridine in the blood, serum, and tissue. The toxic levels of these products cause malfunction of the mitochondrial respiratory chain and mitochondrial DNA. Commonly, patients become symptomatic between 15 and 20 years of age (range 5 months to 35 years). The most commonly affected systems are gastrointestinal, followed by ocular, and nervous system. The disease is often fatal; high mortality rate is reported between 20 and 40 years of age. Treatment modalities that can increase thymidine phosphorylase activity and decrease thymidine and deoxy-uridine have shown symptomatic improvements in patients with MNGIE. Platelet transfusion, hemodialysis, peritoneal dialysis or allogeneic hematopoietic stem cell transplantation (HSCT) have been tried. The survival and long-term benefits of these measures are still not clear. Engrafted patients after stem cell transplantation have showed improvements in serum thymidine and deoxyuridine. We are reporting a case of MNGIE from Saudi Arabia, who underwent allogeneic hematopoietic stem cell transplantation. No MNGIE case has been previously reported from Saudi Arabia or the Gulf Arab countries. From the available literature, so far only 11 patients with MNGIE have undergone stem cell transplantation.

KEYWORDS: Mitochondrial neurogastrointestinal encephalomyopathy; MNGIE; Stem cell transplantation; Bone marrow transplantation

INTRODUCTION

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal recessive disorder characterized by severe muscle wasting, gastrointestinal dysmotility, leukoencephalopathy, peripheral neuropathy, and ophthalmoplegia.[1] The mutations in the ECGF1 gene encoding thymidine phosphorylase (TP) cause alterations in the respiratory chain and mitochondrial DNA (mtDNA).[2] The prognosis of this disease is limited; most patients die by the age of 35 years, but survival may range from 15 to 54 years.[1]

Excessive thymidine alters mitochondrial nucleoside and nucleotide pools leading to impaired mitochondrial DNA replication, repair, or both. There is an assumption that therapies that can reduce thymidine levels might be helpful to MNGIE patients.[3] In a limited number of patients, treatment modalities such as platelet transfusion, hemodialysis, and peritoneal

dialysis or stem cell transplantation were tried. The long-term benefit of these treatments for MNGIE is not clear.[4–6] We report the first case of MNGIE from Saudi Arabia and the Gulf Arab states, and worldwide the 12th case of MNGIE treated with hematopoietic stem cell transplantation (HSCT). However, our patient died on day 24 after transplantation.

CASE REPORT

A 26-year-old male had been suffering from watery diarrhea and abdominal pain over a period of 15 years. There was no history of bleeding per rectum, melena or steatorrhoea. Abdominal pain was scattered all over the abdomen and was mild in severity without any pattern, relieving or aggravating factors. He had difficulty in swallowing on a few occasions. Appetite was normal with no history of fever. The patient was a teetotaler and had no prior sexual exposure or drug addictions. The patient denied history of seizures, headache, arthralgia, chronic cough, chest pain or dyspnoea. He was unmarried and unemployed.

A physical examination showed severe muscle wasting. His body mass index was 12 kg/m^2. The patient was pale. Findings on physical examination included severe sensory and motor peripheral neuropathy of upper and lower limbs; bilateral sensory neural deafness; mild ptosis of the left eye; and ophthalmoplegia. Cardiovascular, respiratory and abdominal examinations were unremarkable.

Patient had consanguineous parents. He had eight brothers and three sisters; two of them had died in road accidents. One sister and another brother died of similar illnesses (chronic diarrhea and muscle wasting). Another sister had chronic diarrhea and muscle wasting, and has been diagnosed with MNGIE. Figure 1 shows the pedigree diagram of the family tree.

On admission, laboratory results were as follows: hemoglobin 104 gm/L (135–180); creatinine 40 µmol/L (64–115); potassium 2.8 mmol/L (3.5–5); calcium 1.3 mmol/L (2.1–2.6); magnesium 0.23 mmol/L (0.70–1); albumin 27 gm/L (32–48); phosphate 0.78 mmol/L (0.8–1.45); lactic acid 4.3 mmol/L (0.5–2); pyruvic acid 217 µmol/L (30–90); ALT 13 U/L (10–45); LDH 306 U/L (135–225); vitamin B6 < 3.5 µgm/L (4.5–60.6); vitamin E 3.5 mg/L (5.5–15.5); copper 2.6 µmol/L (11–22); zinc 10.2 µmol/L (10.6–19); anti tissue trans-glutaminase 8.9 units (0–20); CRP 0.2 mg/L.

Urine thymidine was 72 mmol/mol and plasma thymidine 15289 nano-mols/L (Normal < 700 nano-mols/L). (Baylor Medical Genetics Laboratories; Texas).

The stool examination for ova, parasites, and stool for *Clostridium difficile* were negative. Celiac serology, serum QuantiFERON test, purified protein derivative (PPD) skin test and serology for HIV 1 and 2 were negative. A CT scan of the chest and abdomen with and without contrast showed mild thickening of the terminal ileum, but normal liver, pancreas, adrenals, and other organs. The upper endoscopy showed features of reflux esophagitis. The biopsy from the second part of the duodenum was normal. The colonoscopy revealed narrowed ileocaecal valve, and biopsy from that area and the terminal ileum was normal. The capsule endoscopy was also normal.

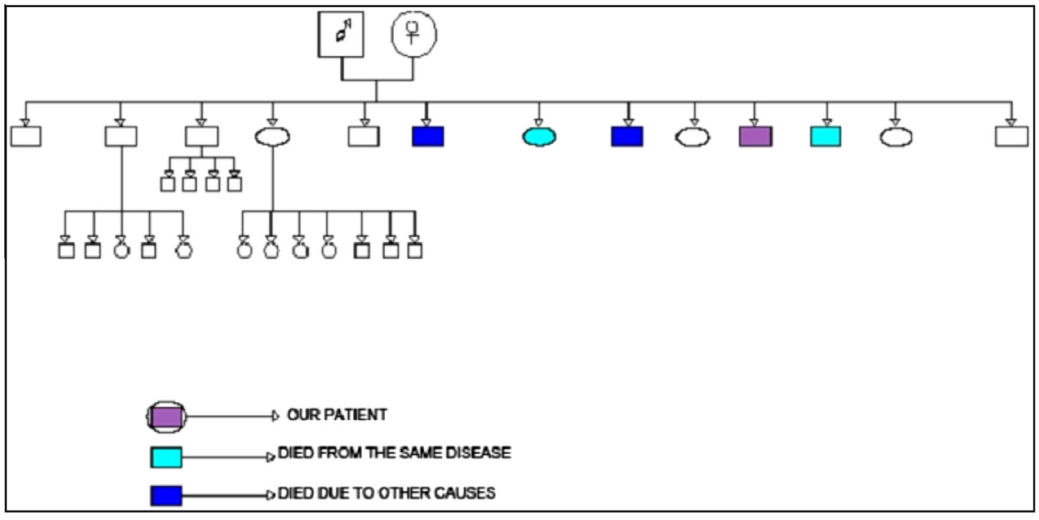

Figure 1. Pedigree diagram of the family tree showing autosomal recessive pattern of inheritance.