Encephalopathy in Type I Hyperlipidemia

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Familial chylomicronemia syndrome is a group of rare genetic disorders characterized by deficient activity of an enzyme lipoprotein lipase or apo-protein C-II deficiency. In this paper we present an infant with massive hyperchylomicronemia and severe pancreatitis. Exchange transfusion for controlling hypertriglyceridemia and pancreatitis led to an increase in hyperviscosity which resulted in encephalopathy.

Key words: *Chylomicronemia, Encephalopathy, Hyperviscosity, Lipoprotein lipase deficiency, Pancreatitis, Plasma exchange.*

Familial chylomicronemia syndrome (type 1 hyperlipoproteinemia) is a rare autosomal recessive inherited disease. The estimated incidence is 1/100000(1,2). Clinically, this condition can be silent and discovered incidentally owing to the lipemic appearance of the blood. But generally it appears during infancy with recurrent abdominal pain. Lipid deposition usually leads to papular eruptive yellow xanthomas over extremities, hepato-splenomegaly and lipemia retinalis. The excessive deposition of chylomicrons may rarely result in encephalopathy and convulsions by disrupting blood circulation due to high viscosity (3).

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Case Report

A 6-month-old male patient was admitted to hospital because of recurrent vomiting, pallor, refusing to feed and constant crying. He was the first child born to healthy, first cousin Turkish parents. His parents had lipid values within normal limits. He was exclusively breast fed since admission. On admission he weighed 5 kg (3rd percentile). He had abdominal distention and tenderness. Hepatomegaly was observed (3 cm below the costal margin). There were no eruptive xanthomas. The patient's serum had a white creamy appearance and the determination of triglycerides in this lipemic sample showed a concentration of 35,000 mg/dL (diluted assay). Cholesterol level was 350 mg/dL. No other biochemical data could be obtained due to the effect of hypertriglyceridaemia on the laboratory results.

Impaired LPL activity with decreased clearance of chylomicrons and VLDL appeared responsible for the hyperlipidaemia in this patient. As a result of these clinical and laboratory findings LPL was the primary diagnosis. The diagnosis was supported by measurement of LPL immunoreactive mass in postheparin plasma (5 ng/mL; normal 220 ± 60 ng/mL). Sequence analysis of the LPL gene is still pending.

Abdominal ultrasound examination revealed pancreatic edema and peripancreatic exudation. Treatment by adequate hydration with lipid free total parenteral nutrition, pain relief and nasogastric suction to manage the persistent vomiting was started. Also, IV carnitine (100mg/kg), omega-3 fatty acids (2 g/d) and vitamin C (200mg/kg/d) were initiated for both antioxidant and triglyceride lowering effects of these agents. At the 3rd day of treatment pancreatitis persisted, triglyceride levels did not decrease (51,300 mg/dL) and tonic and myoclonic convulsions developed which did not respond to phenobarbital and midazolam infusion. As we could not perform plasmapheresis below 30 kg weight because of technical problems, exchange transfusion was initiated with packed red cells and plasma. The packed red cell to plasma ratio was 1:3. On 1st day of exchange transfusion, encephalopathy developed. EEG was consistent with encephalopathy. Cranial magnetic resonance imaging (MRI)

was found normal, without any sign of lipid deposition. The packed red cell used in exchange transfusion was suspected to slow the brain circulation more by increasing the viscosity of the patient's blood which was already high because of its triglyceride content. It was diluted with 0.9% saline solution in a ratio of 1/5. Encephalopathy resolved on the first and pancreatitis resolved on the second day of corrected exchange transfusion. The baby was started to be fed with a fat free diet (basic-f, Milupa, Germany). Continuous blood exchange lasted for 3 consecutive days, and ended after triglycerides level decreased to 800 mg/dL.

During a 12 month follow up on a medium-chained triglyceride based formula and oral 100 mg/kg carnitine, 1000 mg/d vitamin C and 2 g/d omega-3 substitution, triglyceride levels change in range of 300-500 mg/dL. His neurological outcome is normal and the child did not develop any other signs or symptoms.

Discussion

In the present report, we describe a patient with LPL deficiency, who presented with acute pancreatitis and had tonic and myoclonic convulsions despite of treatment with lipid free total IV nutrition, carnitine, omega-3 and vitamin C for 3 days and developed encephalopathy at the first day of plasma exchange transfusion.

The highly abnormal lipid profile pretreatment not responding to medical treatment rapidly, along with pancreatitis would have lead to vascular compromise similar to that seen in neonates with polycythemia and the hyperviscosity syndrome(4). The resultant 'lipid transient ischemia' would have caused the convulsions.

Plasmaphresis is used in patients with severe triglyceridemia who do not respond to medical treatment, especially patients with acute pancreatitis. Lennertz, *et al.* concluded that 1 or 2 TPE sessions sufficed to substantially decrease the bulk of triglycerides in acutely exacerbated chylomicronemia syndrome causing a rapid resolution of acute severe pancreatitis(5,6).

As far as we know exchange transfusion has not been described previously, in the treatment of severe hypertriglyceridemias in children. We had to do exchange transfusion, because of our technical problems in plasmaphresis. Red packed cells and plasma with a ratio of 1:3 was used. It is highly probable that using classical exchange mixture in this ratio, together with the effect of hypertriglyceridaemia not responding to medical treatment led to a much higher viscosity and resulted in encephalopaty in our patient. Encephalopathy has been described in a hyperchylomicronemic infant with apolipo-protein C-II deficiency. As the cranial MRI was normal, our patient differed from this case with severe intracerebral perivascular, extradural lipid depositions, cystic lesions and marked cerebral atrophy(3). Decreasing the viscosity by diluting the exchange solution with normal saline solution resolved the problem immediately and encephalopathy was reversed in one day. Continuing the exchange transfusion led to decrease in triglycerides in three days.

The results we learned from this patient are:

1. Hyperchylomicronemia can lead to convulsions and even encephalopathy in children, especially if the viscosity is more increased for any reason
2. Exchange transfusion is effective in lowering the serum triglycerides. But it must be done cautiously, as exchange itself can cause in an increase in viscosity if inadequate dilutions are used.
3. Encephalopathy can be reversible if there is no lipid deposition in the brain.

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