Hyperlipidemia Due to Rectal Phenobarbital Use: Case Report

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Abstract

Treatment with hepatic enzyme-inducing antiepileptic drugs leads to increases in the levels of total cholesterol (TC) and triglyceride (TG). We report a case of a 10-month-old infant with hyperlipidemia due to use of rectal phenobarbital-paracetamol combination during echovirus infection. To the best of our knowledge, this is the first case reported in the literature of hyperlipidemia due to rectal phenobarbital use.

Introduction

Febrile illness in children younger than 36 months is common and has potentially serious consequences. As parents especially fear the possibility of febrile convulsion; they often administer antipyretics without consulting a physician. Some of these rectal antipyretics are combined with phenobarbital (e.g., Paranox®). Phenobarbital is an antiepileptic known to induce hepatic microsomal enzymes. Microsomal enzyme induction with exogenous drugs can alter the metabolism of bile acids, bilirubin, total cholesterol (TC), triglyceride (TG), and other endogenous molecules [1,2]. A 10-month-old infant presented with hyperlipidemia due to rectal phenobarbital-paracetamol combination (Paranox®), which was used by the parents to reduce fever related to enterovirus infection.

Case Report

The 10-month-old female weighing 10 kg infant presented to our emergency clinic with a five-day history of high fever. There were no previous hospital admissions. The infant was healthy; had received the recommended routine immunizations, and was taking no medications prior to the onset of fevers. Subsequent to the onset of fever; the patient was treated with antipyretics. She appeared good, with a temperature of 38.8°C. Her physical examination was normal; she had a clear oral pharynx, and her tympanic membranes were normal. There was no significant hepatosplenomegaly, lymphadenopathy or skin rash. Cardiovascular and respiratory exams were unremarkable. Her abdomen was soft and nondistended, and normoactive bowel sounds were noted. The neurological exam revealed an awake infant with normal tone, strength, and reflexes. There were no detectable cranial nerve abnormalities. Babinski signs were negative. The initial laboratory data showed normal hemoglobin (13 g/dl), thrombocyte count (365×109/µL) and leukocyte count (10.2×109/µL [neutrophils 34%, lymphocytes 59%, monocytes 7%]). Liver enzymes (aspartate aminotransferase [AST] 15 U/L, alanine aminotransferase [ALT] 41 U/L), renal function tests (urea 9 mg/dl, creatinine 0.2 mg/dl), electrolytes (Na 135 mmol/L, K 4.3 mmol/L, Ca 10.5 mg/dl) and acute phase reactants (C-reactive protein [CRP] 2.97 mg/L, procalcitonin 0.434 ng/ml) were normal. The serum was grossly lipemic. Lipid profile estimation showed markedly increased TG (760 mg/dl) and TC (257 mg/dl) levels. Lumbar puncture was performed, and the cerebrospinal fluid (CSF) analysis was normal. No microorganism was isolated in blood, CSF or urine cultures. Chest X-rays and abdominal ultrasonography were normal. Blood samples were taken for viral serology. While investigating the cause of hyperlipidemia, we learned that the parents had used rectal phenobarbital (15 mg, 3 mg/kg/d)-paracetamol (120 mg, 24 mg/kg/d) combination (Paranox®) twice a day for five days. After stopping the rectal antipyretic treatment, TG (120 mg/dl) and TC (124 mg/dl) levels returned to normal in three days. Echovirus immunoglobulin (Ig)M was eventually detected as positive, and the infant's fever has resolved on the ninth day.

Discussion

Secondary causes of hyperlipidemia include hypothyroidism, nephrotic syndrome, biliary atresia, glycogen storage disease, Niemann-Pick disease, Tay-Sachs disease, systemic lupus erythematosus, hepatitis, and anorexia nervosa [3]. Certain medications exacerbate hyperlipidemia, including isotretinoin, thiazide diuretics, oral contraceptives, steroids, β-blockers, immunosuppressants, protease inhibitors used in the treatment of human immunodeficiency virus (HIV), and anticonvulsants [3-5]. Among these, only the use of anticonvulsant was determined in our patient. Because hyperlipidemia turned up spontaneously normal level, we didn't need to investigate other causes.

Some authors have reported that hepatic enzyme-inducing antiepileptic drugs cause not only long-term increases in serum TC levels, but also short-term increases (over the first year of treatment) in serum levels of TG and TC [4,5]. Sönmez et al. [6] showed that plasma lipoprotein (a) levels were significantly increased during treatment with phenobarbital, carbamazepine, and sodium valproate, and they stated that the results of the studies concerning the effect of antiepileptic drugs on serum lipids are controversial. This is the first case in the literature in which hyperlipidemia was due to rectal phenobarbital use.

In our case, the development of hyperlipidemia in such a short time is remarkable. Yukawa et al. [7] reported that the result indicated that the mean volume of distribution/bioavailability in neonates and infants treated with rectal administration was similar to that obtained in a previous population pharmacokinetic study following intravenous administration [8]. The development of hyperlipidemia in such a short time may be attributed to the rapid increase in serum levels of the drug and the direct involvement of the liver.

In conclusion, the present case indicates that serum lipid profiles

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should be monitored carefully in children receiving phenobarbital.

References


