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Prikaz slučaja
Case report

HYPERLIPIDEMIA TYPE IIB INDUCED ACUTE RECURRENT PANCREATITIS: A CASE REPORT

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Hypertriglyceridemia is a known but underestimated cause of acute pancreatitis. Although the connection between acute pancreatitis and type I, IV, and V hyperlipoproteinemia has been described, using Fredrickson's classification, the connection between type IIb hyperlipoproteinemia and associated pancreatitis has only been reported in a few more rare cases. That is why we present a female patient with recurrent hyperlipidaemic pancreatitis with type IIb hyperlipidaemia.

Keywords: HYPERLIPOPROTEINEMIA, FAMILIAL COMBINED HYPERLIPIDAEMIA, PANCREATITIS, DIABETES MELLITUS

INTRODUCTION

Hypertriglyceridemia (HTG) is a known but underestimated cause of acute pancreatitis and acute recurrent pancreatitis. The manifestation of HTG-induced pancreatitis (HTG pancreatitis) is similar to other causes. A risk factor for acute pancreatitis is a serum triglyceride level of more than 25.9 to 51.8 mmol/L in a patient with type I, IV, or V hyperlipidaemia (Fredrickson's classification) (1). Pancreatitis secondary to HTG is typically seen in the presence of one or more secondary factors (uncontrolled diabetes, alcoholism, medications, or pregnancy) in a patient with an underlying common genetic abnormality of lipoprotein metabolism (familial combined hyperlipidaemia or familial HTG) (2). Although the connection between acute pancreatitis and type I, IV, and V hyperlipoproteinemia of Fredrickson's classification has already been described, connection between type IIb hyperlipoproteinemia and associated pancreatitis has been reported in just a few more rare cases (3, 4). We present a patient with a recurrent episode of pancreatitis associated with type IIb hyperlipoproteinemia.

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CASE REPORT

A 60-year-old woman presented in the emergency room of our hospital complaining of epigastric pain and pain under both costal arches with the expansion in the back for 20 days. She has been admitted to our hospital for the second time due to acute pancreatitis with hyperlipidaemia. She was already diagnosed with type IIb hyperlipoproteinemia nine years before her present hospitalisation. Also, she was diagnosed with NASH (non-alcoholic steatohepatitis) and chronic gastritis. She underwent a hysterectomy due to myoma when she was 45 years old. Seven years before her present hospitalization she was for the first time hospitalised due to acute pancreatitis. Her brother and sister had epilepsy and elevated lipid levels but never took therapy for dyslipidemia. She didn't have xanthoma or xanthelasma. She didn't consume alcohol, and she didn't have biliary calculus. Her height was 178 cm and her weight was 87 kg, with a BMI 27.5 kg/m^2 showing obesity. Even though she was advised low-fat diet and prescribed with drug therapy (fluvastatin, and ezetimibe, and pancreatic enzymes), she deliberately stopped taking the prescribed medication without special reason. On her physical examination, her abdomen was slightly painful on a deep palpation with hypoactive bowel sounds, and she had direct tenderness on the epigastrium with a rebound phenomenon. On admission, laboratory data showed a white blood cell count of 6.6 x 10^9/L (3.4-9.7 x 10^9/L). A blood chemistry test revealed a lactate dehydrogenase level of 278 U/L (25-241 U/L), serum lipase level of 222 U/L (13-60 U/L), serum amylase level of 60 U/L (23-91 U/L). Serum alanine aminotransferase levels of 42 U/L, aspartate aminotransferase levels of 89 U/L and gama-glutamyltransferase levels of 1012 U/L (8-35U/L). Serum calcium level was low 1.8 mmol/l (2.44-2.53 mmol/l), and phosphate levels were also low 0.77 (0.79-1.42 mmml/l). Her lipid profiles, such as serum total cholesterol (TC) and triglyceride level (TG) were 24.4 mmol/L (<5 mmol/L) and 24.8 mmol/l (<1,7 mmol/L), receptively, but levels of high-density cholesterol (HDL) and low-density cholesterol (LDL) could not be measured in the laboratory. While taking blood for analysis, it is important to note that the blood was turbid and creamy. It took more than 10 hours to analyse lipid profiles. Dietary restriction and hydration were started immediately after hospitalization. Plasmapheresis was the first therapy option, but after a blood chemistry test, therapy was started with 24000 units of heparin in 500 ml of 0.9% physiological saline for 24 hours and 8 units of fast-acting insulin in 10% glucose solution for 12 hours. The next day lipid profile levels were measured again. Levels of TC, TG, HDL, LDL were 11.9 mmol/L, 4.7 mmol/L, 1.56 mmol/l (>1.2 mmol/L) and 9.42 mmol/L (<3 mmol/L), respectively, with normalisation of hepatic enzymes. After 3 days, statin therapy was re-introduced. Abdominal CT scan revealed normal density but enlarged liver and spleen (17.5 cm and 14 cm respectively).

Abdominal MR showed signs of oedema of the pancreatic tail. Post-contrast imbibition showed no signs of necrosis. Surrounding fatty tissue showed increased densities with free liquid peripancreatic fluid, and all in terms of acute pancreatitis. Her abdominal pain was resolved within a few days, and she was discharged after 10 days with a complete recovery from acute pancreatitis.

DISCUSSION

The mechanism by which hypertriglyceridemia leads to pancreatitis was suggested by Havel et al (5). Hypertriglyceridemia can be a consequence of increased VLDL (very low-density lipoprotein) production, decreased VLDL and/or chylomicron catabolism, or most likely both these mechanisms. As a result, hyperglyceridaemia results in an increase in high serum TG level in the following types of lipoproteins: 1) VLDL (familial hypertriglyceridemia, known as Fredrickson type IV hyperlipoproteinaemia (HLP), or familial combined HLP, or HLP type IIb, in which LDL cholesterol level is also increased); 2) VLDL and chylomicrons (HLP type IV); 3) VLDL remnants and chylomicron remnants (dysbetalipoproteinaemia, also known as remnant disease or HLP type III); and 4) chylomicrons only (HLP type I) (6). The most frequent is familial hypertriglyceridemia (5-10% of the population), which is related to various genetic factors and secondary factors superimposed on genetic susceptibility, including environmental factors, leading to VLDL overproduction. Serum TG level is usually in the range of 5.18-12.95 mmol/L. Less frequent polygenic hypertriglyceridemia (1-2% of the population) include familial combined hyperlipoproteinemia which results from an increased hepatic synthesis of apolipoprotein B (apo B), leading to an increase in VLDL production (7). An even less frequent condition is dysbetalipoproteinaemia (0.01% of the population) (7). If TG level exceeds 5.6 mmol/L, and in particular 11.3 mmol/L, lipoprotein lipase (LPL) becomes saturated by VLDL triglyceride, and chylomicrons appear in plasma in fasting condition (8). By this mechanism, fasting chylomicronaemia may develop in familial hypertriglyceridemia, familial combined hyperlipidaemia, and dysbetalipoproteinaemia, leading to HLP type V.

The most severe complication of severe hypertriglyceridemia (SHTG) with fasting chylomicronaemia is acute pancreatitis. SHTG is the third-common cause of acute pancreatitis after alcohol abuse and cholelithiasis, and it is responsible for up to 10% of all episodes of acute pancreatitis (9). It is interesting that the rates of SHTG among patients with acute pancreatitis in 3 prospective studies were 12%, 21%, and 22% (10). Although the threshold TG level for an increased risk of pancreatitis has not been defined, it is often arbitrarily set at >11.3 mmol/l. The exact mechanism for acute pancreatitis due to SHTG is not known. It has been assumed that high local levels of free fatty acids (FFA) released by pancreatic lipase during the hydrolysis of TG present in chylomicrons exceed the binding capacity of albumin and include inflammation (11). According to another hypothesis, increased chylomicron levels lead to excessive plasma viscosity, resulting in hypoxia and local acidosis in pancreatic capillaries, which increases the toxicity of FFA (12).

Our patient has been treated for acute pancreatitis in two occasions. Serum lipoprotein electrophoresis was done in the first hospitalisation, but not in the second. However on the first admission, serum levels of TG were 7.8 mmol/L, and on second admission they were >24 mmol/L which was not compatible with the belief that hyperlipidaemic pancreatitis is associated with a serum triglyceride level of more than 25 mmol/L and advice that controlling of TG levels to 12,9 mmol/L or less can effectively prevent recurrences of pancreatitis (1, 2, 7). The risk of acute pancreatitis in patients with serum triglycerides >24 and 51 mmol/L is ~ 5% and 10% to 20%, respectively (2). FDA-approved treatments include HMG-CoA reductase inhibitors (statins), fibric acid derivatives (fibrates), bile acid sequestrants, PCSK9 inhibitors, adenosine triphosphate-citrate lyase inhibitors (bempedoic acid), niacin, and ezetimibe. Other treatment options include omega-3 fatty acids (fish oil) and MTTP inhibitors (lomitapide) (13, 14).

Our patient didn't take therapy or follow a low-fat diet for more than nine months, and despite that, she didn't develop acute pancreatitis. It is not clear whether HTG pancreatitis is more severe than when it is due to other causes. Clinical management of HTG pancreatitis is similar to pancreatitis of other etiologies. Insulin infusion in diabetic patients with HTG can rapidly reduce triglyceride (TG) levels, Even though our patient wasn't diabetic, we conducted the same therapy. Better-designed studies are required for the clarification of plasmapheresis in the treatment of HTG pancreatitis, because the use is still experimental (2).

Familial combined hyperlipidaemia is one of the most common hereditary lipid disorders that affects at least two family members. Despite its prevalence and potential health consequences, it is often underdiagnosed and undertreated (15). Although acute pancreatitis is a rarely described complication, earlysdiagnosis, and treatment of this hyperlipoproteinemia are necessary, assis screening of family members.

For sure, accurate and fast diagnosis with diet, lifestyle changes, and medications is important for the treatment and prevention of recurrent HTG pancreatitis and the long-term management of TG levels.

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Sažetak

AKUTNI REKURENTNI PANKREATITIS IZAZVAN HIPERLIPIDEMIJOM TIP IIB: PRIKAZ SLUČAJA

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Hipertrigliceridemija je poznat, ali podcijenjen uzrok akutnog pankreatitisa. Iako je već opisana veza između akutnog pankreatitisa i hiperlipoproteinemije tipa I, IV i V, korištenjem Fredricksonove klasifikacije, veza između hiperlipoproteinemije tipa IIb i pridruženog pankreatitisa zabilježena je samo u još nekoliko rijetkih slučajeva. Upravo zbog toga prikazujemo pacijenticu s rekurentnim hiperlipidemijskim pankreatitisom s hiperlipidemijom tipa IIb.

Ključne riječi: HIPERLIPOPROTEINEMIJA, OBITELJSKA MJEŠOVITA HIPERLIPIDEMIJA, PANKREATITIS, DIJABETES MELITUS

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