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Case Report

Oral Contraception-induced Hypertriglyceridemic Pancreatitis: A Case Report of A Rare But Still Present Complication

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Abstract

All estrogens-containing birth control pills will increase fasting serum triglyceride levels. This is an estrogenic dose-dependent increase and is reflected by an increase in very low-density lipoprotein-VLDL mainly due to an increased hepatic production of triglycerides. Although estrogens administration also elevates serum triglycerides in most patients without pre-existing hyperlipidemia, these increases are generally very mild and are not associated with pancreatitis. We present a case of 24-year woman who was treated for acute pancreatitis as a consequence of hypertriglyceridemia associated with oral contraceptive pills.

Keywords: Acute pancreatitis; Hypertriglyceridemia; Oral contraceptive pills

Introduction

Used by millions of women around the world, oral contraception is considered a safe method of birth control however, it has side effects. One of the rare complications is acute pancreatitis. The first two cases were published in 1970 (by Bank and Marks) [1, 2]. In these two cases, as well as in cases that were reported later, the serum triglyceride levels were considerably high during the acute pancreatitis episode and normalized soon after the withdrawal of oral contraception [3]. Many studies have shown that estrogens therapy can considerably elevate serum triglyceride levels in patients with pre-existing lipid abnormality, as for example hyperlipoproteinemia types IV and V (Fredrickson classification based on electrophoretic pattern) [4]. In women with moderately elevated serum triglyceride levels combined with elevated levels of very low density lipoproteins (VLDL) type IV hyperlipidemia is often the case. These women are typically moderately obese with impaired glucose tolerance and a positive family history of diabetes and hyperlipidemia [4, 5]. In such women oral contraception can cause a fast increase of serum triglyceride level which can be higher than 11.3mmo/l in 2-4 weeks [5]. The effect of oral contraception on the elevation of triglyceride levels depends on the estrogens dosage and is affected by the increase of VLDL, which is caused by the elevated production of triglycerides in the liver [5]. Furthermore, hypertriglyceridemia is the cause of up to 7% of all cases of acute pancreatitis [6]. In the absence of other etiologic factors hypertriglyceridemic acute pancreatitis is defined by the presence of elevated triglyceride levels (>11.3mmol/l) and lactescent serum [7].

The purpose of this case report is to point out oral contraception as a rare but still possible cause of hypertriglyceridemic acute pancreatitis.

Case Report

A 24-year old woman, a smoker with no concomitant diseases, was admitted for acute pancreatitis. On the day of admission she was suffering from epigastric pain and vomiting, she had no fever or chills. On admission her blood pressure was 110/70mmHg, her abdomen was soft, with epigastric tenderness, the liver and spleen were not palpable and her BMI was 29.6kg/m^2. In the four months prior to admission she had been taking oral contraceptive pills Diane 35® (ethinyloestradiol 35mcg, cyproterone acetate 2mg). She had just completed her menstrual cycle and had started bleeding three days before admission.

On admission her serum was macroscopically hyperlipemic. The laboratory results showed leucocytosis (12.5x10^9/l), elevated blood sugar (9.9mmol/l), mildly elevated C-reactive protein (CRP) (20mg/l), elevated serum lipase (30.6mckat/l) and amylase (1.8mckat/l), mildly elevated gama glutamil transferase (0.85mckat/l), normal levels of transaminases, elevated serum triglycerides level (26.8mmol/l), elevated cholesterol level (8.3mmol/l), lowered high-density lipoprotein level (HDL) (0.79mmol/l), as well as lowered low-density lipoprotein level (LDL) (2.0mmol/l).

An abdominal ultrasound showed liver steatosis, edematous pancreas, peripancreatic oedema but no focal lesions of the pancreas, the gallbladder was empty, no dilatation of the extra hepatic and intra hepatic biliary ducts was seen. The patient was fasted and treated with a crystalloid infusion, a glucose infusion with insulin, an analgetic therapy and a proton pump inhibitor. With increasing CRP levels to 243mg/l on the third day of hospitalization we decided to treat her with parenteral antibiotics (ciprofloxacin and metronidazol). The patient improved after a few days and the triglyceride level dropped to 6.4mmol/l, on discharge (on the seventh day of hospitalization) the cholesterol level was 7.96mmol/l, HDL 0.53mmol/l, LDL 4.5mmol/l. She was put on gemfibrozil and advised to discontinue the oral contraception.

Discussion

The mechanism by which hypertriglyceridemia leads to

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pancreatitis is not clear. A well-accepted mechanism is that hydrolysis of triglycerides by pancreatic lipase leads to the accumulation of free fatty acids in high concentrations [6, 8]. The pancreas contains a high concentration of enzyme lipase that hydrolyses triglycerides to glycerol and free fatty acids, which are normally bound to albumin. High local concentrations of free fatty acids may develop, which leads to saturation of albumin binding with the release of large amounts of cytotoxic free fatty acids in the pancreatic circulation [9]. Unbound free fatty acids can produce acinar cell or capillary injury [6]. Chylomicrons are formed 1-3 hours after the meal and are normally eliminated in 8 hours. When the level of serum triglycerides is more than 11.3mmol/l the chylomicrons are permanently present [8]. An increased concentration of chylomicrons causes the plugging of pancreatic capillaries, which leads to ischemia and acidosis [6, 9-12]. In the acidotic environment, free fatty acids cause activation of trypsinogen and initiate acute pancreatitis [6].

Acute pancreatitis with hypertriglyceridemia usually occurs when triglyceride levels are >11.3mmol/l but it is uncertain how long these levels must be sustained [9].

The increase in triglyceride production is also connected with the effect of circulating estrogen on the level of circulating insulin and growth hormone [4]. The growth hormone induces the adipose tissue lipolysis and consequently increases the concentration of free fatty acids, which are used for liver synthesis of triglycerides, which is stimulated by insulin [4]. As reported by Perseghin estrogen-containing oral contraceptives can produce a 40% reduction of insulin sensitivity associated with increased level of free fatty acids, cholesterol, and triglycerides [13, 14].

In general estrogens elevate the serum triglyceride concentration, which depends on estrogen dosage, and nortestosteron derivates tend to reduce serum triglyceride levels [3, 4]. In patients with no pre-existing hyperlipidemia the serum triglycerides increase is usually mild and does not lead to pancreatitis [4].

''In most of the reported cases acute pancreatitis has occurred within three months after starting estrogen therapy. Abdominal pain and pancreatitis have ceased within 10 days after estrogen therapy withdrawal'' [4]. Besides increase of the serum triglycerides level, mild increase of serum cholesterol and fasting glucose level have also been noted [4]. Probably an elevated level of insulin is required for hypertriglyceridemia as the diabetic patients with low insulin level do not develop pancreatitis after estrogen therapy [4].

There is a relative contraindication for estrogen therapy in patients with primary hyperlipidemia. In patients with obesity, diabetes, or a family history of diabetes or hyperlipidemia, low dose estrogen and/or gonane progestagen therapy is recommended [3].

Estrogen-induced increases of HDL and triglycerides are opposed by progestin, in the order from least to greatest effect: dydrogesterone and metrogestone, progesterone, cyproterone acetate, medroxyprogesterone acetate, transdermal norethindrone acetate, norgestrel, and other norethindrone acetate [13, 15].

The clinical course of acute pancreatitis after estrogen therapy is usually mild to moderate. Usually there is a short episode of abdominal pain and a moderate to severe increase of pancreatic enzymes and triglycerides, which normalize soon after estrogen withdrawal [10, 15]. In the two cases reported by Glueck in 1994 the course of the acute pancreatitis was severe, the computer tomography imaging showed pancreatic oedema [10, 16]. Recently, Abraham M et al. reported a severe acute pancreatitis in a young woman taking norethindrone acetate/ethinyl estradiol for almost 10 years, who was treated in intensive care unit [17].

In the case of our patient there were two problems – she was overweight and had hyperglycaemia. However, we did not take the information on her family history of diabetes and hyperlipidemia. Her alcohol consumption was negligible, we found no gallstones and there was no injury vascular or autoimmune disease which could be the cause of hyperlipidemic acute pancreatitis. As in previously published cases [4], the acute pancreatitis in our patient developed at the end of the menstrual cycle. With the discontinuation of the oral contraceptive therapy, the level of triglycerides dropped quickly.

Conclusion

In a young, healthy women taking oral contraception, who is presenting with acute abdominal pain, the possibility of acute pancreatitis should be considered. As there have been just single cases of oral contraception-induced hypertriglyceridemic pancreatitis reported, we cannot recommend the routine measurements of lipids during oral contraception intake. However, in case of obese person or family history of hyperlipidemia the lipid level checking could be helpful in preventing acute pancreatitis.

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