JOP. J Pancreas (Online) 2004; 5(5):353-356.

CASE REPORT

Estrogen-Induced Severe Acute Pancreatitis in a Male

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ABSTRACT

Context Acute pancreatitis is related to drugs in 1.4-2% of cases. Estrogens are an uncommon but well-known risk factor of pancreatitis in women and men with pre-existing hyperlipidemia.

Case report We report the case of a 37-year-old man with covert hypertriglyceridemia who developed a severe life-threatening pancreatitis strongly associated with estrogen therapy preparatory to sex change surgery, characterized by a massive triglyceride level, pancreatic insufficiency and multiple organ failure at the time of the diagnosis. Other causes of the disease were ruled out.

Conclusions To our knowledge, this is the first description of severe necrotizing estrogen-induced pancreatitis in a male. Baseline abnormal triglyceride levels should be checked by physicians before starting estrogen therapy in women and men.

INTRODUCTION

Pancreatitis secondary to hypertriglyceride-mia is a rare but well-known disease. A pre-existing lipoprotein abnormality along with the presence of a secondary trigger factor can lead to a serum triglyceride level of more than 1,000 to 2,000 mg/dL and represents a risk factor for the development of acute pancreatitis [1]. Exogenous estrogens have been shown to increase both triglyceride and high density lipoprotein levels. A recent study comparing the effect of estrogens and a placebo on lipoproteins reports a definite but non-significant elevation in triglyceride levels during estrogen treatment in postmenopausal healthy women who were randomized to receive estrogens, estrogens plus progesterone or a placebo, but no cases of pancreatitis were reported [2]. In a small selected group of patients, exogenous therapy can lead to mild to severe pancreatitis. A retrospective study showed that 39% of women who received hormonal replacement treatment had pre-existing, usually covert, familial hypertriglyceridemia: in this population, the estrogen-induced elevation of triglycerides was marked and led to pancreatitis in 4 of the 7 patients whose triglyceride levels were greater than 1,500 mg/dL [3]. The literature reports a strong link between estrogen replacement therapy or contraceptive therapy, hypertriglyceridemia and mild to severe pancreatitis [4, 5]; however, only one case of a man in postprostatectomy estrogen therapy, who actually developed mild acute pancreatitis with a moderate triglyceride increase, has been reported [4]. We report a case of severe necrotizing pancreatitis characterized by massive hypertriglyceridemia due to a high–dose estrogen therapy preparatory to sex change surgery in a young man with pre-existing covert hyperlipidemia.

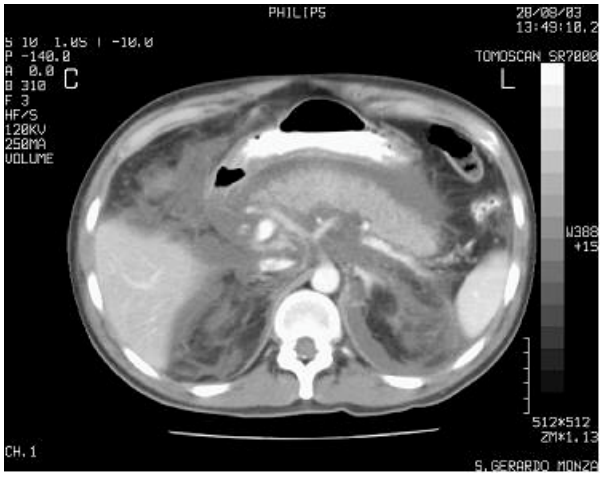

Figure 1. Extensive enlargement of the pancreas with peripancreatic fluid (2nd day of hospitalization).

CASE REPORT

A 37-year-old man was referred to the Emergency Room of San Gerardo Hospital in August 2003 with a sudden onset of severe epigastric pain, nausea and vomiting. The abdomen was tender and resistant to palpation, particularly in the upper quadrants and no bowel sounds were present. He had no history of previous abdominal surgery or previous diagnosis of gastroduodenal ulcer, gastritis or pancreatitis. The results of the examination were non-specific but a diagnosis of pancreatitis was supported by an amylase value of 1,842 IU/L (reference range: 0-100 IU/L) and an abdominal ultrasound showing an extensive enlargement of the pancreas. No evidence of gallstones, biliary tree dilatation or obstruction were revealed. No history of alcohol abuse was found. Blood tests revealed a marked increase of triglyceride level (5,174 mg/dL, reference range: 50-200 mg/dL), total cholesterol level (773 mg/dL, reference range: 130-200 mg/dL) and glucose (453 mg/dL, reference range: 70-110 mg/dL). There was no family history of hyperlipidemia or diabetes. For two months prior to admission, estrogenic and antiandrogenic compounds (conjugated estrogens 0.625 mg, cyproterone 2 mg, and ethinyl estradiol 0.035 mg) had been administered every day for three months by the family physician as a complementary treatment preparatory to sex change surgery. The family physician had not recognized the estrogen therapy as being the cause of the recurrent abdominal pain in the month prior to the acute onset of the symptoms and, consequently, the estrogen treatment was suspended the day of the hospitalization itself. The patient was managed with supportive therapy, nasogastric suction, intravenous rehydration, analgesic and antiproteasic medications. An abdominal CT scan was performed the next day, showing extensive pancreatic edema, mesenteric edema and the presence of peripancreatic fluid and fluid in the pelvic space. A diagnosis of severe acute pancreatitis was made. In the days following admission, triglyceride, cholesterol and amylase levels started to reverse slowly despite the worsening of the abdominal tenderness, and pain and the development of severe hypoxemia and respiratory insufficiency (PO_2: 54 mmHg; 0_2 saturation: 87%). A new CT scan showed bilateral pleural effusion and a massive increase in peripancreatic fluid, and paracolic and retrocavity fluids (Figures 1 and 2). Antibiotic therapy was added as well as insulin therapy for a persisting high glucose level (453 mg/dL). Bilateral pleural drains were required and a blood transfusion was necessary owing to anemia (hemoglobin 9.5 g/dL, reference range: 14.0-18.0 g/dL; hematocrit 28.6%, reference range: 41.0-53.0%). Blood tests on the tenth day showed a progressive regression towards the normal values of triglyceride,

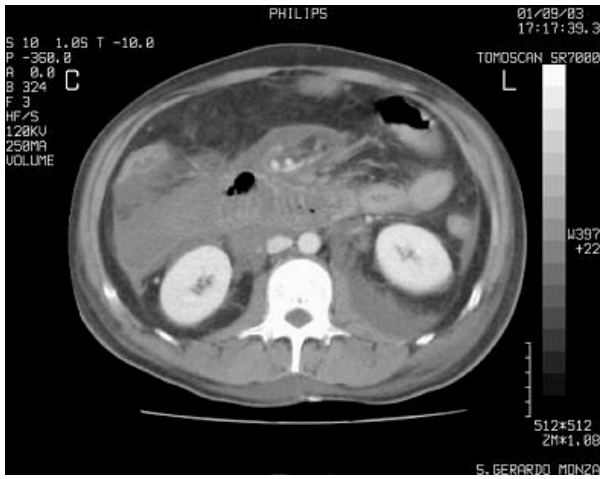

Figure 2. Multiple necrotic areas and complete alteration of the glandular structure (8th day of hospitalization).

amylase and glucose levels (223 mg/dL, 29 UI/L, and 275 mg/dL, respectively). Successively, his clinical condition slowly improved. The patient started to eat on the 22nd day after admission with no episodes of vomiting or pain. Intravenous fluids and antibiotics were discontinued soon after. At the time of discharge, blood tests revealed triglyceride, glucose and amylase levels within the reference ranges (181 mg/dL, 154 mg/dL, and 47 UI/L, respectively). A mild pleural effusion was still present at CT scan, as well as a slight pancreatic edema and massive peripancreatic fluids which subsequently decreased. It was recommended that he not take estrogens any longer. The patient was discharged in apparently good physical condition. The patient was admitted to the hospital twice in the following seven months for abdominal pain and subocclusion, but his clinical condition soon improved with medical therapy, and the laboratory abnormalities all reversed quickly.

DISCUSSION

The literature linking estrogens to pancreatitis has been reported scanty in the last twenty years [3, 4, 6]. There is clear evidence which supports this association, despite the fact that the exact mechanism remains uncertain; estrogens, particularly when unopposed by progesterone, can increase triglyceride levels through reduced triglyceride-clearing enzymes and increased endogenous triglyceride synthesis [7]. This abnormality has no clinical importance in most of the populations taking estrogens but in the presence of pre-existing hypertriglyceridemia the increase can be exponential and lead to a dangerous accumulation of toxic free fatty acids resulting from the hydrolysis of the triglycerides by pancreatic lipase [8]. Acinar cell injury, capillary plugging and subsequently pancreatic ischemia and acidosis are all possible when the triglyceride level is greater than 1,000 mg/dL. A case of estrogen-induced pancreatitis in the setting of normal plasma lipids has recently been described suggesting that another estrogen-related mechanism may be responsible for pancreatic inflammation [9]. In the case we report, the evidence supporting the etiologic role of estrogen-inducing massive hypertriglyceridemia and pancreatitis seems very strong. There was no history of alcohol use and no family history of pancreatitis. There was no evidence of gallstone disease and the patient was not taking other medications. The symptoms occurred just two months after starting the estrogen therapy and resulting in massive hypertriglyceridemia associated with the onset of the pancreatitis. The situation was ameliorated when the estrogens were discontinued..

Hyperlipidemic pancreatitis due to estrogens has been commonly studied in female populations receiving hormone replacement therapy or birth control pills and having pre-existing hyperlipidemia, and only in one case of a hypertriglyceridemic man receiving estrogen therapy after prostatectomy for cancer. Acute pancreatitis due to estrogens is usually described as mild to moderate with short episodes of abdominal pain without pancreatic insufficiency, associated with a moderate to high increase of amylase and triglyceride levels which usually return to within the range of normality as soon as the therapy is discontinued. In only two women studied by Glueck in 1994 was the acute pancreatitis severe with CT scan evidence of pancreatic edema and the occurrence of severe hypoxemia [3].

We described severe hyperlipidemic acute pancreatitis in a man with covert hypertriglyceridemia under estrogen treatment preparatory to sex change surgery. A markedly abnormal triglyceride level (5,174 mg/dL) at the time of the diagnosis, the CT scan evidence of massive peripancreatic fluids and multiple pancreatic necrotic areas and the development of severe respiratory insufficiency and important anemia make this the most severe case of pancreatitis due to estrogens described so far.

Men, as well as women, with a baseline elevated triglyceride level (greater than 750 mg/dL) should be considered at high risk for developing acute pancreatitis if estrogen

therapy has been planned. Physicians should check potentially covert hyperlipidemia in order to avoid the serious complication of estrogen-induced pancreatitis.

Received May 21st, 2004 - Accepted June 6th, 2004

Keywords Hormones /therapeutic use; Multiple Organ Failure; Pancreatitis, Acute Necrotizing

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