CASE REPORT

Acute pancreatitis owing to very high triglyceride levels treated with insulin and heparin infusion

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SUMMARY

Hypertriglyceridaemia is the third most common cause of acute pancreatitis in the USA. The treatment approach for hypertriglyceridaemia to date has largely been conservative including weight loss, exercise and avoidance of medications that raise triglyceride levels. This approach, however, is not practical in cases of acute pancreatitis due to severely elevated triglycerides. A small number of case reports have been published supporting the treatment of acute pancreatitis due to severely elevated triglyceride levels with insulin and heparin. We report a case of acute pancreatitis in a young woman due to a triglyceride level of 15 215 mg/dl who was successfully treated with insulin and heparin.

were 351 and 589 units/l, respectively. Serum sodium was 122 meq/l, potassium 3.5 meq/l and glucose 323 mg/dl. Thyroid function tests were within the normal range. Her total cholesterol was 1034 mg/dl with a TG level 15 215 mg/dl. Using Friedewald equation, low-density lipoprotein (LDL) could not be quantitated due to very high TG levels. Urinalysis and ECG were unremarkable. Ultrasound of the abdomen was suggestive of inflammatory changes in the pancreas, but with normal gallbladder and biliary tree. A CT scan of the abdomen showed moderate inflammation surrounding the pancreas with a small amount of fluid in the anterior pararenal space consistent with acute pancreatitis.

BACKGROUND

An estimated 1–4% of acute pancreatitis cases are caused by triglyceride (TG) levels in excess of 1000 mg/dl. Hypertriglyceridaemia-induced acute pancreatitis (HTGP) is thought to manifest with increased severity as compared to pancreatitis due to other causes.¹ HTGP has significant morbidity and mortality if reduction in TG levels is not achieved. Prompt treatment with insulin and heparin has been shown to improve outcome.² Our case highlights the importance of management of severe HTGP with insulin and heparin infusions.

CASE PRESENTATION

A 31-year-old woman presented to the emergency department with acute epigastric abdominal pain radiating to her back with associated nausea of 8 h duration. She denied any vomiting, fever and dysuria. Her medical history was significant for obesity (body mass index 45 kg/cm²), hyperlipidaemia on dietary management, hypertension and uncontrolled type II diabetes mellitus. She had no history of alcohol, tobacco or drug abuse. Her medications included acetaminophen, enalapril and insulin. Physical examination revealed a temperature 37°C, blood pressure 162/104 mm Hg and oxygen saturation 95% on room air. Abdominal examination revealed marked epigastric tenderness with sluggish bowel sounds. No abdominal masses or organomegaly were noted. Tendon xanthomas and xanthothesma were absent. Heart and chest examinations were within normal limits and she was neurologically intact.

INVESTIGATIONS

Laboratory studies revealed leucocytosis 15 215/mm³, haemoglobin 12 g/dl, platelet count 233 000/mm³ and normal liver enzymes. Her amylase and lipase

TREATMENT

A diagnosis of acute pancreatitis due to very high levels of TGs was made. Treatment with intravenous fluids and narcotics for pain relief was started. Insulin and heparin infusions were also initiated for very high TG levels and then continued for 5 days. Intravenous regular insulin (0.4 U/kg/h) without dextrose was titrated to a blood sugar less than 200 mg/dl. A heparin infusion was titrated for a target partial thromboplastin time of less than 100 s. TG levels trended down to 1185 mg/dl on day 4 and then to 363 mg/dl on day 6 of admission. She was discharged on gemfibrozil and statin therapy on day 6 of admission (figure 1).

OUTCOME AND FOLLOW-UP

She remained asymptomatic with normal TG levels on a 6-month follow-up. The cause of

Figure 1 Trend of triglyceride (TG) levels with treatment.

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hypertriglyceridaemia (HTG) was presumed to be from uncontrolled diabetes and obesity.

DISCUSSION

HTG refers to TG levels above 150 mg/dl with levels exceeding 1000 mg/dl considered to be very high. HTG is the third most common cause of acute pancreatitis after gallstones and alcohol. Acute pancreatitis may be induced when TG levels exceed 1000 mg/dl.³ Most patients with high levels of TGs have some form of primary or genetic defect in lipid metabolism. Acquired causes of HTG include uncontrolled diabetes mellitus, obesity, hypothyroidism, end-stage renal disease, nephrotic syndrome, HIV and medications such as isotretinoin, tamoxifen and oestrogen.⁴ The pathogenesis by which high TG cause pancreatitis is not fully understood. It is postulated that the pancreas secretes a high concentration of the digestive enzyme lipase, which hydrolyses TGs to glycerol and free fatty acids. These free fatty acids are non-toxic to the pancreas as long as they are bound to the albumin. When TG levels are very high and albumin becomes saturated, however, accumulation of free fatty acids may develop locally in the pancreas. This can lead to cytotoxic reaction along with vascular endothelial damage causing pancreatic ischaemic injury and inflammation.²

Clinical presentation of HTGP is similar to other forms of pancreatitis. A family history of high TG levels may be present. Physical examination should focus on the signs of HTG (eruptive xanthomas over extensor surfaces of arms, legs or back, xanthelasma, lipaemia retinalis and hepatosplenomegaly from fatty infiltration of the liver). As in our case, high TG levels can confound the measurement of sodium and LDL (using Friedewald equation: $LDL = \text{total cholesterol} - \text{high-density lipoprotein (HDL)} - \text{TG}/5$). The excess TG in a serum sample can displace water containing sodium and can cause pseudohyponatremia. Although our patient had high amylase levels, TG levels greater than 500 mg/dl can falsely cause normal amylase levels, as it interferes with the calorimetric reading assay end point. In such cases, serial dilutions of the serum amylase sample or measurement of lipase can be helpful.¹

Many options have been suggested for the treatment of HTGP including the traditional method of dietary restriction of TG-containing foods and using lipid-lowering medications.⁵ Our treatment approach was based on a series of case reports that have demonstrated efficacy of insulin and/or heparin. In addition to lowering the overall costs, this approach is minimally invasive and reduces the likelihood of having to undergo plasmapheresis to rapidly lower TG levels.

Insulin activates lipoprotein lipase, thereby accelerating TG's degradation into fatty acid and glycerol, and also facilitates storage in adipocytes.⁶ Intravenous insulin may be given as a continuous infusion starting with 0.1–0.3 U/kg/h with titration as required to maintain blood sugar levels between 150 and 200 mg/dl. Similar to insulin, heparin enhances lipoprotein lipase activity by stimulating the release of endothelial lipoprotein lipase into circulation.⁷ Antihyperlipidaemic agents such as gemfibrozil 600 mg twice daily can be used as adjuvant therapy to enhance lipoprotein lipase activity.⁸ If this approach was unsuccessful, plasmapheresis can be attempted to directly remove lipoprotein particles that act as potential triggers for continued damage to the pancreas.⁹ The reduction in TG levels by more than 50% in our case of HTGP by using insulin and heparin was seen in 3 days which was similar to 2.8 days described by Henzen *et al.*⁸

Though the severity and complication of pancreatitis (pancreatic abscess formation, necrosis, organ dysfunction and sepsis) have been found to be more common in HTGP, death rates are similar to other aetiologies of pancreatitis. Interestingly, the severity of pancreatitis does not seem to correlate with TG levels. There is no clear evidence as to which HTG patients will develop pancreatitis and whether HTGP may cause chronic pancreatitis in the long term.¹⁰

In summary, after reviewing the available literature and analysing the outcomes of our own case, the most reasonable approach for managing patients admitted to an acute care facility for acute pancreatitis due to very high (greater than 1000 mg/dl) TG levels consists of dietary restrictions, fluid resuscitation and therapy with insulin and heparin.

Learning points

- ▶ Triglyceride (TG) levels greater than 1000 mg/dl may induce hypertriglyceridaemia-induced acute pancreatitis (HTGP).
- ▶ HTGP usually responds to insulin and/or heparin infusion. It is minimally invasive and reduces the likelihood of having to undergo plasmapheresis to rapidly lower TG levels.
- ▶ The goal of such treatment is to lower TG level to less than 500 mg/dl.
- ▶ Though the severity and complication of pancreatitis have been found to be more common in HTGP, death rates are similar to other causes of pancreatitis.

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Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Tsuang W, Navaneethan U, Ruiz L, *et al.* Hypertriglyceridemic pancreatitis: presentation and management. *Am J Gastroenterol* 2009;104:984–91.
- 2 Alagözli H, Cindoruk M, Karakan T, *et al.* Heparin and insulin in the treatment of hypertriglyceridemia-induced severe acute pancreatitis. *Dig Dis Sci* 2006;51:931–3.
- 3 Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP). Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* 2001;285:2486–97.
- 4 Yuan G, Al-Shali KZ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. *CMAJ* 2007;176:1113–20.
- 5 Poonuru S, Pathak SR, Vats HS, *et al.* Rapid reduction of severely elevated serum triglycerides with insulin infusion, gemfibrozil and niacin. *Clin Med Res* 2011;9:38–41.
- 6 Goldberg IJ. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. *J Lipid Res* 1996;37:693–707.
- 7 Twilla JD, Mancell J. Hypertriglyceridemia-induced acute pancreatitis treated with insulin and heparin. *Am J Health Syst Pharm* 2012;69:213–16.
- 8 Henzen C, Röck M, Schnieper C, *et al.* [Heparin and insulin in the treatment of acute hypertriglyceridemia-induced pancreatitis]. *Schweiz Med Wochenschr* 1999;129:1242–8.
- 9 Jain P, Rai R-R, Udawat H, *et al.* Insulin and heparin in treatment of hypertriglyceridemia-induced pancreatitis. *World J Gastroenterol* 2007;13:2642–3.
- 10 Ewald N, Hardt PD, Kloer H-U. Severe hypertriglyceridemia and pancreatitis: presentation and management. *Curr Opin Lipidol* 2009;20:497–504.

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