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CASE REPORT

Acute management of hyperlipaemic pancreatitis: a successful reduction in triglyceride levels with simultaneous insulin infusion and plasma exchange

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We report on a case in which a combination of an insulin infusion and plasma exchange were successfully used in the acute management of hyperlipaemic pancreatitis.

Keywords: acute pancreatitis, anti-TNF agent, AP, hyperlipaemic pancreatitis, hypertriglyceridaemia, infliximab, insulin infusion, plasma exchange

Introduction

Acute pancreatitis (AP) is an infrequently encountered potentially fatal complication of severe hypertriglyceridaemia, with a 5% mortality rate.[1] Hypertriglyceridaemia is the causative factor in up to 7% of cases of AP, and the third most common cause after alcohol and gallstones.[2,3] Few case reports have been published on the specific modalities in the acute management of hyperlipaemic pancreatitis. The role of modalities, such as insulin and heparin, as well as plasma exchange, in the management of severe hypertriglyceridaemia is not yet clear. We report on a case in which concurrent insulin and plasma exchange was a successful treatment modality in the acute management of hyperlipaemic pancreatitis.

Case study

A 32-year-old female patient, known to have psoriatic arthritis, presented with a two-week history of severe epigastric pain radiating to her back, accompanied by nausea, vomiting and fever, and a history of starting the anti- tumour necrosis factor (TNF) agent, infliximab, two months before presentation. She had been diagnosed with pancreatitis two weeks prior to admission to our facility. During admission, the infliximab was discontinued and the patient improved. She was a smoker and reported that her father had had a fatal myocardial infarction aged 40 years. There was no specific mention of familial hypertriglyceridaemia. She was not diabetic. The patient was not pregnant and denied alcohol use. A physical examination revealed epigastric tenderness. There was no eruptive xanthoma, nor hepatosplenomegaly. The laboratory investigation revealed serum amylase levels of 562 IU/l (normal 25–125 IU/l), serum lipase levels of 777 IU/l (normal 13–60 IU/l), urine amylase levels of 3 611 IU/l (normal 0–490 IU/l), C-reactive protein levels of 2.1 mg/l (normal < 5.0 mg/l), serum triglycerides of 60.5 mmol/l (normal 0.4–1.6 mmol/l) and normal liver function. Urine pregnancy testing was negative. Computed tomography (CT) showed oedema of the pancreas with excessive phlegmon formation, free fluid in the pelvis and bilateral pleural effusions (Figure 1). There were no signs of stones in the biliary ducts, nor any ductal dilatation.

A diagnosis of severe hypertriglyceridaemia complicated by AP was made. The anti-TNF agent was implicated as the most likely underlying cause. The patient was admitted to the intensive care unit, where she received an insulin infusion and two sessions of plasmapheresis, in addition to standard therapy for AP which included intravenous analgesia and rehydration. She was made to fast for two days, after which she followed an extremely low-fat diet. Her triglyceride levels decreased to 4.5 mmol/l within three days, at which point bezafibrate was introduced at 400 mg per day (Figure 2.) Infliximab was not reintroduced.

Discussion

Patients with triglyceride levels of ≥ 11.3 mmol/l are at risk of developing AP.[4] Five per cent of these patients develop AP as a result of the hypertriglyceridaemia.[5] Many factors contribute to pancreatic damage in patients with triglyceride levels in excess of 11.3 mmol/l. The leakage of pancreatic lipase causes hydrolysis of the triglycerides and degradation of the chylomicrons, forming proinflammatory free fatty acids, leading to endothelial damage. Chylomicrons are large triglyceride-rich lipoproteins, and when present in large quantities can interfere with pancreatic capillary blood flow owing to hyperviscosity, thereby leading to ischaemic changes in the acini. This process leads to accelerated pancreatic tissue necrosis.[5,6] Hyperlipaemic pancreatitis is a potential complication of primary (genetic), as well as secondary, disorders of lipid metabolism. Secondary hypertriglyceridaemia has been documented in the presence of a number of conditions, including diabetes mellitus, pregnancy, hypothyroidism, excessive alcohol intake and nephrotic syndrome, as well as the use of a number of drugs, including hormone replacement drugs, selective oestrogen receptor modulators, certain antiretroviral agents, retinoids, thiazides, beta blockers and propofol.[7]

Although conventional interventions in AP are of paramount importance, specific therapies for acute severe hyperlipaemic pancreatitis are still unclear. Supportive therapy of any AP aetiology includes aggressive hydration, analgesia, nutritional support, restriction of the exogenous triglycerides and monitoring in a high care environment.[8] Proposed specific modalities in the acute management of hyperlipaemic pancreatitis include plasma exchange and the use of heparin and insulin.[9,10] However, consensus guidelines do not exist, randomised control studies are lacking and experience is limited to case reports.

The goal of acutely lowering triglyceride levels in hyperlipaemic pancreatitis is to prevent complications, such as necrotising

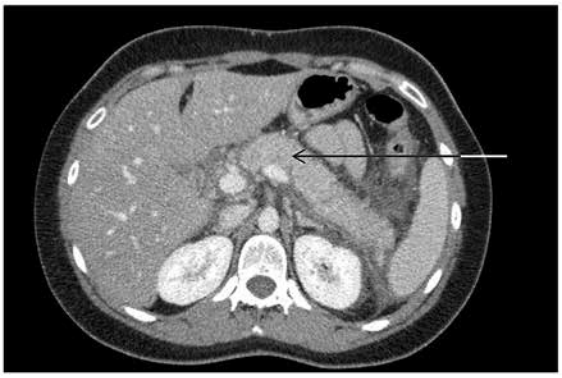
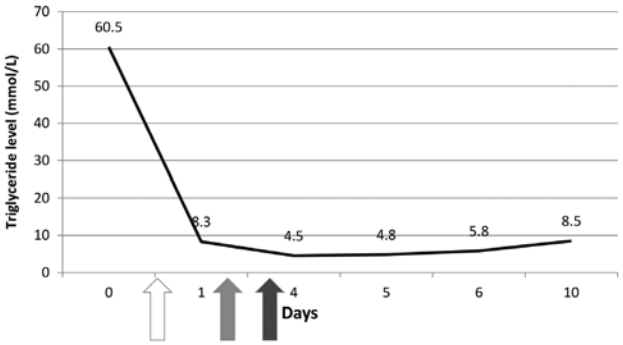


Figure 1: A computed tomography scan of the abdomen, showing oedema of the pancreas, particularly the head of the pancreas (arrow) with phlegmon formation and free fluid in the abdomen, favouring a radiological diagnosis of acute pancreatitis.



Note: The first session of plasma exchange and insulin infusion were commenced within 12 hours of the diagnosis (white arrow). The second session of plasma exchange was performed at 36 hours (grey arrow). Bezafibrate was introduced on day 3 (black arrow).

Figure 2: The rapid decline in serum triglyceride levels in response to specific modalities.

pancreatitis, organ failure and death. First-line drugs, such as fibrates, omega-3 fatty acids, statins and niacin, do not lower triglyceride levels rapidly, owing to their slow onset of action. For this reason, the early initiation of specific interventions, including the use of heparin, insulin infusions and plasma exchange, has been recommended.

Both insulin and heparin stimulate the release of lipoprotein lipase (LPL), therefore decreasing levels of circulating triglycerides. Many no longer favour the use of heparin, as the effect on increasing LPL activity has been shown to peak transiently, and ultimately result in a decrease in LPL activity, leading to raised triglyceride levels.[5]

Plasma exchange is an extracorporeal method, employed to rapidly remove triglycerides from the circulation, thereby preventing the formation of free fatty acids. The removal of toxic proteases is another postulated benefit of plasma exchange.[11] The early initiation of plasma exchange was revealed to deliver the best results in a few retrospective analyses.[12,13] In 2014, Gubensek et al. conducted an observational study in which 111 episodes of hyperlipaemic pancreatitis in 103 patients were analysed. They found that plasma exchange reduced triglyceride levels within the first two days. This was found to occur sooner than both conservative management and treatment with heparin and insulin. A low complication and mortality rate was also demonstrated.[1]

Although the use of plasma exchange in rapidly lowering triglyceride levels has been described in many case reports, the number of plasma exchange sessions required to lower triglyceride levels remains unclear.[1,14] Taking all the available published literature into consideration, we elected to treat our patient with a combination of an insulin infusion and two sessions of plasma exchange, where we removed 3 *l* of plasma, and replaced it with 5% human albumin, without fresh frozen plasma. The plasma exchange was initiated within 12 hours of presentation, in addition to the standard management of AP, and achieved a 74% reduction in triglyceride levels within 72 hours. Both insulin infusion and plasma exchange are effective in acutely lowering circulating triglycerides. However, experience with the concomitant use of plasma exchange and insulin is limited. We concede that there is uncertainty as to which therapeutic modality resulted in the rapid reduction of serum triglycerides in our patient. Head-to-head trials are required which compare the use of insulin infusion alone, plasma exchange alone, and a combination of the two, to establish evidence-based guidelines on the acute management of this life-threatening condition. A significant lowering of triglyceride levels by Gaudet et al., using a selective antisense inhibitor of apolipoprotein C-III (ApoCIII), was demonstrated in a very recent publication.[15] They achieved a mean reduction in triglyceride levels of 71% after 13 weeks of the subcutaneous administration of the antisense inhibitor of ApoCIII.

Conclusion

A new modality in the treatment of patients with severe hypertriglyceridaemia who are at risk of serious complications, including hyperlipaemic pancreatitis, is now available. However, long-term data and head-to-head comparisons with existing modalities are required.

Conflict of interest – The authors declare no conflict of interest.

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