Acute pancreatitis secondary to hypertriglyceridaemia caused by undiagnosed type 2 diabetes

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Abstract

In some patients undiagnosed diabetes may present with metabolic complications of diabetes as their initial presentation. Suboptimal glycaemic control in diagnosed and undiagnosed diabetes can cause hypertriglyceridaemia which can cause pancreatitis. In patients presenting with pancreatitis where common causes of pancreatitis are excluded hypertriglyceridaemia should be considered as a cause and hence their lipid profile should be evaluated. If hypertriglyceridaemia is confirmed, then such a patient should be screened for diabetes. We present three cases presenting to hospital with pancreatitis secondary to hypertriglyceridaemia. Hypertriglyceridaemia in all three were secondary to undiagnosed and uncontrolled type 2 diabetes. Early treatment of hypertriglyceridaemia can prevent morbidity and mortality. Diagnosing type 2 diabetes in this context can result in optimisation of glycaemic control, and hence improve hypertriglyceridaemia and reduce the risk of recurrent attacks of pancreatitis.

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Introduction

The incidence of type 2 diabetes is rising sharply. According to recent statistics, 463 million people across the world have type 2 diabetes, whilst approximately 232 million are undiagnosed.[1] Although many undiagnosed patients may experience no or subtle symptoms of diabetes, many patients may present with atypical manifestations. Apart from the classical symptoms of hyperglycaemia, people with undiagnosed type 2 diabetes can present with metabolic complications. Hypertriglyceridaemia is a known metabolic complication of poor glycaemic control in both diagnosed and undiagnosed type 2 diabetes and can lead to acute pancreatitis.[2,3] Timely recognition and aggressive management can achieve rapid control of hypertriglyceridaemia and avoid considerable morbidity and mortality.

Case presentation

We present three patients (A, B and C) who were fit and well with no known medical comorbidity. All had family history of type 2 diabetes. All presented with sudden, severe abdominal pain associated with vomiting. Patient characteristics and biochemical results on admission to hospital are shown in Table 1. All three were diagnosed with acute pancreatitis and had a serum sample that was lipaemic (Figure 1) on visual inspection with significantly elevated triglyceride levels. None of the three patients had gallstones or any other hepatobiliary pathology on abdominal ultrasound. There was no history of alcohol intake and they had normal serum calcium levels, hence there was no other obvious cause of pancreatitis. All three had high capillary blood glucose levels on admission to hospital, but none of them as per investigation results had diabetic ketoacidosis. Primary hypothyroidism was ruled out as a cause for hypertriglyceridaemia with normal thyroid stimulating hormone (TSH) levels. All patients had no antecedent history of hyperglycaemic symptoms or weight loss. Glycosylated haemoglobin (HBA1c) levels for all three patients were significantly higher than the cut-off currently used for diagnosing diabetes, and hence confirming the diagnosis of undiagnosed type 2 diabetes. Abdominal computed tomography (CT) scans for all patients showed changes consistent with acute pancreatitis with no liquefaction or gross destruction of pancreatic tissue.

All three patients were managed conservatively with standard evidence-based supportive treatment for acute

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Figure 1 Lipemic serum sample

pancreatitis which included fluid resuscitation, analgesia and nutritional support. All were treated with intravenous insulin (regular insulin) infusion with the addition of dextrose infusion once blood sugar levels were below 200 mg/dL to avoid hypoglycaemia. Triglycerides levels started to decline sharply with insulin infusion (Table 2) and all patients made a swift recovery. None of the patients required surgical intervention. All were discharged from hospital within a week on subcutaneous insulin injections for their diabetes along with gemfibrozil. They were kept under regular Endocrine follow-up, and all were gradually weaned off insulin and switched to oral hypoglycaemic agents after 2–3 months once glycaemic control was optimised and triglyceride levels were stabilised (Table 2). Hypertriglyceridaemia was clinically driven by suboptimal glycaemic control (with undiagnosed type 2 diabetes) and hence remained stable and settled with rapid optimisation and maintenance of stable glycaemic control. Gemfibrozil was switched to statins for long-term cardiovascular protection because all patients were at high cardiovascular risk according to their periodic lipid profile, HbA1c assessment and regular home blood glucose monitoring. Lipid profiles remained stable with optimal glycaemic control and none of the three patients to date have had any recurrent episode of pancreatitis.

Discussion

A proportion of people with undiagnosed diabetes may not have classic diabetes symptoms, and such patients may present with a metabolic complication of uncontrolled diabetes in the form of pancreatitis caused by hypertriglyceridaemia as their first presentation with diabetes.

Fasting serum triglyceride levels of >150 mg/dL is defined as hypertriglyceridaemia. Severity is classified based on the level of triglyceride elevation as follows:[4]

- 150–199 mg/dL is mild
- 200–999 mg/dL is moderate
- 1,000–1,999 mg/dL is severe
- ≥2,000 mg/dL is very severe

Hypertriglyceridaemia causes up to 14% of acute pancreatitis.[5] Pancreatitis risk increases with increasing severity of hypertriglyceridaemia. The risk of pancreatitis is about 5% when serum triglycerides levels are >1,000 mg/dL and rises to about 10–20% with triglyceride levels >2,000 mg/dL.[6]

Primary (genetic) and secondary disorders of lipoprotein metabolism can cause hypertriglyceridaemia.[7] Suboptimal glycaemic control in diagnosed and undiagnosed type 1 and type 2 diabetes can cause hypertriglyceridaemia, and therefore hypertriglyceridaemia-induced pancreatitis.

Table 1 Patient characteristics and biochemical results on admission to hospital

Patient	Age	Sex	BMI	Triglyceride (mg/dL) <150 mg/dL	Serum amylase 30–110 U/L	HbA1c mmol/mol	TSH 0.4–4 mU/L	Serum calcium 8.5–10.5 mg/dL
A	44	Female	33	2,985	169	91.3	3	9
B	39	Male	23	6,720	1587	71.6	0.9	10
C	35	Female	34	10,930	750	65	2	8.7

Table 2 Serial triglyceride and HbA1c levels

Patient	Triglyceride level (mg/dL)					HbA1c mmol/mol	
	Day 1	Day 2	Day 3	Day 5	3 months	Admission	3 months
A	2985	1223	850	372	200	91.3	58.5
B	6720	3080	819	224	180	71.6	53
C	10930	7940	1004	725	300	65	51.9

Absolute and relative lack of insulin causes lipolysis with free fatty acid formation. High levels of free fatty acids in circulation result in increased synthesis and release of very low-density lipoproteins from the liver which, together with reduced activity of peripheral tissue lipoprotein lipase, results in hypertriglyceridaemia.[8] Toxic free fatty acids are produced by the breakdown of triglycerides by pancreatic lipases. These fatty acids are the cause of lipotoxicity in pancreatitis.[9]

Pancreatitis caused by hypertriglyceridaemia is usually more severe than other causes of pancreatitis.[7,10] Triglyceride levels >500 mg/dL may cause false-normal amylase levels, making biochemical confirmation of diagnosis of pancreatitis difficult. Serial dilution of the serum sample may be required to overcome this interference.[11]

The mainstay of treatment in hypertriglyceridaemia-induced pancreatitis is either therapeutic plasma exchange or intravenous insulin whilst investigating for a cause of hypertriglyceridaemia. If a cause is found, then specific treatment of the cause is continued in parallel.[12–14] Intravenous insulin usually lowers triglycerides to <500 mg/dL over 3.5–4 days, has more efficacy than subcutaneous insulin in severe cases and is equally effective in patients with or without diabetes. Insulin lowers triglyceride levels by enhancing activity of lipoprotein lipase and inhibiting activity of hormone sensitive lipase.[15] Intravenous insulin optimised hypertriglyceridaemia and hyperglycaemia in all three cases in this series.

Once triglycerides are <500 mg/dL, patients will require long-term pharmacological therapy along with dietary modification to prevent recurrent attacks.[16] If a secondary cause like diabetes is found, then maintaining adequate glycaemic control can prevent recurrent pancreatitis.

Conclusion

Patients presenting with acute pancreatitis should be screened for hypertriglyceridaemia in the absence of common causes of pancreatitis. If confirmed, diabetes screening should be undertaken if the patient is not known to have diabetes because suboptimal glycaemic control is a recognised cause of hypertriglyceridaemia in diagnosed and undiagnosed diabetes. Rapid optimisation of hypertriglyceridaemia can reduce morbidity and mortality.

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