CASE REPORT

Acute pancreatitis and severe hypertriglyceridaemia masking unsuspected underlying diabetic ketoacidosis

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SUMMARY

A healthy 18-year-old girl presented to a local emergency room with 48 h of abdominal pain and vomiting. A radiological and biochemical diagnosis of moderate acute pancreatitis was made. Bloodwork demonstrated prominent hypertriglyceridaemia (HTG) of 19.5 mmol/L (severe HTG: 11.2–22.4), detectable urine ketones and a random blood glucose of 13 mmol/L dropping to 10.5 mmol/L on repeat (normal random <11). Ketone levels were deemed consistent with fasting ketosis after 48 h of vomiting. There was no known history of diabetes in the patient. Management included aggressive rehydration and pain control, yet the patient rapidly decompensated into shock requiring intensive care unit support. Blood gases revealed severe metabolic acidosis (pH 6.99) and unsuspected underlying diabetic ketoacidosis was diagnosed. The HTG gradually resolved following intravenous fluids and insulin infusion with slower correction of the metabolic acidosis. Importantly, her glycated haemoglobin was 12%, indicating the silent presence of chronic glucose elevations.

BACKGROUND

This case highlights an error in diagnosis due to an incompletely considered differential diagnosis for severe hypertriglyceridaemia (HTG). The recognition of acute pancreatitis (AP) arising secondary to the triglyceride elevations was appropriate, yet the failure to identify the underlying cause of the HTG led to subsequent patient collapse and shock. This emphasises the necessity of considering and actively screening for serious underlying causes of the HTG itself, such as the silent and profound insulin deficiency and resulting severe diabetic ketoacidosis (DKA) present in this case. Improving awareness of this clinical association will enhance detection and management of its complications through prompt recognition and treatment of the DKA.

In addition, this case brings to light the diagnostic considerations of the temporal order and reciprocal impact of insulin deficiency and AP, as either can be an aetiological trigger for the other. Specifically, DKA can be associated with secondary acute pancreatitis due to HTG from profound insulin depletion. The reciprocal, however, is also true. A sequelae of severe AP is exocrine but also endocrine pancreatic damage resulting in impairment of insulin producing β -cells and secondary insulin deficiencies resulting in DKA.

CASE PRESENTATION

After 48 h of anorexia, nausea and non bloody vomiting at home, the patient presented to her

local hospital where the diagnosis of moderate AP was made based on an abdominal CT and ultrasound and serum chemistry. Ongoing symptoms, including left upper quadrant, 7/10 stabbing pain, with generalised abdominal cramps, led to her transfer to the closest tertiary hospital for further management.

Upon admission to the tertiary hospital, the patient was treated as an uncomplicated pancreatitis. Immediate management included IV rehydration therapy, antiemetics, and narcotics for pain control with further orders for nothing to be ingested until the patient was re-evaluated.

Initial assessment of the patient showed a temperature 37.3°C, heart rate 110 bpm, blood pressure 126/68 mm Hg, respiratory rate 14 breaths/min, and an oxygen saturation of 98% on room air. She had a normal body habitus and was not in distress, however, she was experiencing a moderate amount of abdominal discomfort. Her physical examination showed no xanthasmas or skin eruptions, nor was a fruity odour detected. Her gastrointestinal examination showed diffuse tenderness, with a soft, non-distended abdomen. Also, there was no organomegally noted. Other than tachycardia, her cardiorespiratory examination was unremarkable with the notable absence of tachypnoea.

The patient was previously healthy without any medical history or surgical history. Her medication list was limited to the oral contraceptive pill (ethinyl oestradiol, norgestimate). The patient describes only occasional social alcohol consumption (none within the last week) and no binge drinking or recreational drug use in the past. There were no recent surgeries, gastrointestinal endoscopic procedures or abdominal trauma. She denies fever, chills, rigours or recent unintended weight loss. There was no history of polyuria or polydipsia. She did not have any prodromal abdominal symptoms. There had been no similar episodes previously. There was no family history of dyslipidemias, pancreatitis or gallstones. Her family history was significant for rectal carcinoma in her paternal grandfather and type 2 diabetes in her maternal grandmother.

Six hours after her arrival at our tertiary hospital, and 12 h from her first presentation and assessment at the local rural hospital, the patient began to decompensate with rapid progression of hypotension, tachycardia and tachypnoea. The acute decompensation to hypotension and shock was assumed to be due to progression of the pancreatitis with potential infection complicating the pancreatitis. The patient was aggressively rehydrated and started on

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broad spectrum antibiotics. However, the hypotension failed to respond to fluid resuscitation and there was increased patient distress. She was urgently consulted to the intensive care unit (ICU) for supportive measures and management.

INVESTIGATIONS

A community abdominal ultrasound was performed on her initial presentation to her local rural hospital showed a normal gallbladder and liver with normal intrahepatic and extrahepatic bile ducts. An abdominal non-contrast CT was consistent with moderate pancreatitis, and demonstrated greater involvement of the pancreatic body and tail, compared to the head. The CT also showed significant fat stranding and some fluid exudates with an hypoechoic area within the body of the pancreas. The gallbladder, liver, spleen and biliary tree were reported as normal.

Laboratory investigations drawn on arrival at the tertiary hospital were significant for a normal urea and creatinine in a very lipemic sample. The liver enzymes including alkaline phosphatase, γ -glutamyltransferase, alanine transaminase, aspartate aminotransferase and total bilirubin were within normal ranges, however, amylase was elevated at 319 U/L. The complete blood count showed an elevated white cell count of $15.1 \times 10^9/L$. Random glucose was 13 mmol/L. The most striking abnormality, however, was a marked elevation of triglycerides (19.48 mmol/L, normal <2.25 mmol/L) and total cholesterol (19.47 mmol/L, normal <5.1 mmol/L). Her corrected calcium was normal at 2.15 mmol/L. Bicarbonate levels were not obtained.

On her subsequent decline into shock 12 h later, further emergent tests included an arterial blood gas which was grossly abnormal with an acidic pH of 6.99, PCO_2 9.4, PO_2 134, and HCO_3 of 5.4. The serum bicarbonate level was low at 15 mmol/L and the calculated anion gap was elevated at 22 (normal 8–16). Random glucose was 15 mmol/L.

DIFFERENTIAL DIAGNOSIS

The causes of acute pancreatitis are extensive and include structural, metabolic and toxic aetiologies (table 1). In this case, cholelithiasis or other obstructive causes were ruled out by the imaging studies performed and her history was not forthcoming for toxin exposure or alcohol ingestion, infections, trauma or drug induced. The obvious trigger for the AP in this case appeared to be the severe HTG.

There is an extensive list of causes for HTG that include metabolic, genetic and pharmacological causes. Upon her arrival

and following her initial assessment, her current use of a contraceptive pill containing oestrogen remained as a potential aetiological cause of the triglyceride elevations particularly as there was no known family history of dyslipidemias to suggest a genetic susceptibility to this.

TREATMENT

The arterial blood gas results requested on transfer to ICU made it very clear that the decompensation was linked with a significant anion gap metabolic acidosis. Quantitative ketones were tested and found elevated, and the diagnosis of severe DKA was confirmed. An insulin infusion was initiated and maintained for 3 days with correction of the metabolic acidosis, HTG and normalisation of the ketones and anion gap.

OUTCOME AND FOLLOW-UP

The patient spent 6 days in the ICU and 2 days in the general ward before being discharged home with the diagnosis of HTG-induced pancreatitis and type 1 diabetes mellitus (DM1) complicated by DKA. She was started on basal with prandial bolus subcutaneous insulin therapy and recommended to not restart her oral contraceptive pill until stable triglyceride levels were confirmed on repeat testing. She was scheduled to follow-up with her local outpatient endocrinology service and lost from our service. At the time of discharge her triglyceride levels had returned to normal (3.2 mmol/L) as had her cholesterol levels.

DISCUSSION

This case allows us to present a medical error and a complex diagnosis. This type of medical error has been referred to as ‘anchoring bias’ when a diagnosis is locked onto too early, and there is a failure to adjust to new information. The reported absence of tachypnoea at her initial presentation may have been misleading as it firmly goes against acidotic states. This may have been a medical error in vital sign assessment or the patient was truly not yet in active DKA and still compensating with her existing pancreatic insulin reserve. The presence of ketones and mild glucose elevations very early in the presentation was not investigated further and was rationalised away. In retrospect, the glucose levels should have been considered to be fasting samples given her complete anorexia for 48 h prior to testing. In this light, diabetes would have been very strongly suspected and DM1 considered given her slender build, young age and positive ketones at presentation.

This was a first-presentation of DM1. The patient had likely been hyperglycaemic for some time given the remarkable elevations of her glycated haemoglobin at 12%. Given her lack of prodromal symptoms, she was in a honeymoon phase of her DM1 yet able to partially compensate for the declining insulin levels. It interested us to know if it was likely that the acute pancreatitis led to the rapid development of DKA through pancreatic damage. A literature review has helped us to understand the most likely order of events resulting in her acute pancreatitis and DKA.

First, it is well established that insulin regulates lipoprotein lipase, resulting in an anabolic storage of triglycerides into adipose tissue. A true lack of insulin dysregulates this process and can result in elevated levels of serum triglycerides, as had presumably occurred in our young woman. Looking at the literature, it is clear that triglyceride levels can rise to high enough levels to significantly increase the risk of acute pancreatitis in individuals diagnosed with DKA, with reported triglyceride levels from 11 to 100 mmol/L.^{2–6} This makes it very plausible that the high triglycerides observed in the patient were from lack of insulin and triggered her pancreatitis.

Table 1 Aetiologies of acute pancreatitis (AP), with incidence rates¹

Etiology of AP	Incidence (% of AP cases)
Gallstone	35–40
Alcohol	30
Hypertriglyceridaemia	1–4
Post-ERCP	3–25 (of ERCP procedures)
Idiopathic	15–25
Hypercalcemia	1.5
Drug induced	0.3–1.4
Infection (viral (most common), bacterial, fungal)	<1
Trauma	<1
Pregnancy	<1
Genetics (cystic fibrosis CFTR gene)	<1
Toxins	<1

ERCP, endoscopic retrograde cholangiopancreatography.

Secondly, it is known that AP, as well as chronic pancreatitis, can damage pancreatic exocrine and endocrine function.^{7–12} How commonly, therefore, does acute pancreatitis result in transient or permanent damage of pancreatic endocrine function, or even DKA? There have been several case series and small case-control studies examining degrees of insulin insufficiency after AP (glucose intolerance and DM). One report comparing severe versus mild AP shows the rate of pancreatic endocrine insufficiency after 42 months of follow up were a striking 79% and 44%, respectively.⁷ A case series published in Poland¹³ followed 47 alcoholic AP patients after 4 years and found that a high rate of glucose intolerance (12.8%) and overt insulin dependant diabetes (17%) was present. These reports make it very plausible that the acute pancreatitis in the patient may have caused a precipitous drop in her remaining β -cell population leaving her profoundly hypoinsulinemic with a rapid development of DKA.

A case series of three middle-aged DKA patients published in the AJG (September 1997) with elevated triglyceride levels (ranging between 7.1 and 19.2 mmol/L) and CT-diagnosed AP concluded that DKA was the inciting event triggering the pancreatitis.² This series of cases differs from ours as the patients described were long standing diabetics rather than a first-presentation-DM1. However, they still show that low insulin states can lead to HTG and subsequently AP. The pathophysiological difference in our case was the possible existence of residual insulin reserve (rather than established deficiency) that was rapidly lost following the development of AP and its associated inflammatory damage to β cells. In our case, the rapid normalisation of triglyceride levels with insulin replacement goes against a heritable dyslipidemia contributing to her presentation.

Learning points

- ▶ As with masked acute pancreatitis (AP) in cases of diabetic ketoacidosis (DKA), there is definite risk for masked DKA in cases of AP, especially with young adult patients without any other risk factors for AP.
- ▶ Be aware of the common cognitive error of search satisfaction where the search for other problems is stopped when one diagnosis is made. Anchoring is another cognitive error that can lead to search satisfaction. This is a tendency to rely too heavily on one piece of information when making decisions.
- ▶ The pathophysiology of hypoinsulinemic states causing hypertriglyceridaemia is common, typically in poorly controlled type 2 diabetic patients. As with our case, it is also certainly possible in a prolonged honeymoon phase in a previously undiagnosed type 1 diabetic patient.

Contributors Both authors contributed to writing, referencing and editing of the case report.

Competing interests None.

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