Reminder of important clinical lesson

Abdominal pain and hyperamylasaemia—not always pancreatitis

Sally Slack,¹ Ianthe Abbey,² Dominic Smith²¹ Department of Clinical Biochemistry, York Hospital, York, UK² Department of Paediatrics, York Hospital, York, UK

Correspondence to Sally Slack, sally.slack@york.nhs.uk

Summary

A raised serum amylase concentration, at least four times the upper limit of normal (ULN), is used to support the diagnosis of acute pancreatitis in a patient presenting with abdominal pain. The authors report a case of toxic shock syndrome complicated by a raised serum amylase concentration that peaked at 50 times the ULN in a patient with recurrent abdominal pain. The commonest cause of hyperamylasaemia is pancreatic; however, further investigation of serum lipase and amylase isoenzyme studies found this to be of salivary origin and attributable to soft tissue inflammation of the salivary gland. This case highlights the need to consider non-pancreatic causes of hyperamylasaemia.

BACKGROUND

The clinical diagnosis of pancreatitis is supported by the finding of a high serum amylase, and levels greater than 10 times the upper limit of normal (ULN) are often considered to be virtually diagnostic. This case serves as an important illustration that not all cases of hyperamylasaemia are associated with pancreatitis and it is essential that a salivary gland source of amylase is considered where appropriate. Many cases of hyperamylasaemia of salivary origin have been reported with modestly raised amylase concentrations (up to 15× ULN). This case is unique in showing how salivary pathology should be considered as the source of amylase even when levels exceed 50 times ULN.

CASE PRESENTATION

A 15-year-old was admitted from primary care to the children's ward with a 1-day history of fever, a sore throat and abdominal pain.

The past medical history included two recent admissions for severe right iliac fossa pain, associated with anorexia and nausea. During the first admission, 6 months previously, a diagnostic laparotomy was performed, which revealed a ruptured physiological ovarian cyst. During the second admission, 1 week previously, a laparoscopic appendectomy was performed. Histological analysis showed a normal appendix with a small left-sided fimbrial cyst. Of note, during the previous admissions there was no significant abnormality in routine blood testing and serum amylase was 61 U/L (reference interval 1–100) on the first admission.

INVESTIGATIONS

On examination the patient was hypotensive (blood pressure 80/60), feverish with a temperature of 39.4°C, the tonsils were covered in white pus and the tongue was also coated. The soft tissue of the face was oedematous. The abdomen was tender and a faint blanching erythematous rash was observed. The patient rapidly developed signs of

shock with poor capillary refill and despite fluid resuscitation the patient remained hypotensive.

Initial blood results indicated a neutrophilia with a white blood cell count of $21.4 \times 10^9/\text{litre}$ (reference interval 4–11), creatinine of 312 $\mu\text{mol}/\text{litre}$ (reference interval 45–84) and amylase of 2472 U/litre (reference interval 1–100). Blood gas analysis showed a profound metabolic acidosis with a pH of 7.14 (reference interval 7.35–7.45) and HCO_3^- of 9.7 mmol/litre (reference interval 21–31).

DIFFERENTIAL DIAGNOSIS

The patient was transferred to the intensive care unit (ICU) with presumed pancreatitis, systemic inflammatory response syndrome and multi-organ failure. The acidosis worsened and the pH decreased to 6.90. Toxic shock syndrome was considered in the differential diagnosis and swabs were taken from the throat and the laparoscopy site.

TREATMENT

Ultra filtration renal replacement was initiated and the patient was treated with very high doses of inotropes, cefotaxime, metronidazole, clindamycin and hydrocortisone. Immunoglobulin and activated protein C were also administered.

OUTCOME AND FOLLOW-UP

The serum amylase peaked at 4977 U/litre on day 2 on ICU and was initially assumed to be of pancreatic origin. It was not clear whether this was primary or secondary to shock. An abdominal ultrasound was requested, which showed a normal pancreas, liver and biliary tree. At this time it was considered that the amylase may not be of pancreatic origin, especially as at presentation the patient had clinical evidence of significant inflammation of the tonsils and mouth. Amylase isoenzymes were requested as well as serum lipase. The serum lipase was reported at 12 U/litre (reference interval 22–51) and the isoenzyme studies showed the increase in amylase to be entirely of the salivary isoform;

the pancreatic amylase isoform was reported as <5 U/litre. The serum amylase concentration decreased to 52 U/litre by day 7 on ICU.

The swab taken from the laparoscopic operation site subsequently showed growth of *Staphylococcus aureus*. This isolate tested positive for the gene encoding toxic shock syndrome toxin 1 confirming the diagnosis of toxic shock syndrome.

The patient required intensive care treatment for 16 days prior to extubation and was discharged home after a further 6 days of rehabilitation care on the paediatric ward.

DISCUSSION

Hyperamylasaemia remains the most commonly used biochemical marker for the diagnosis of acute pancreatitis. However, the clinical specificity of this marker for pancreatic disease can be as low as 61% depending on the patient population studied as many other intra-abdominal and salivary gland pathologies result in a raised concentration.¹

Two amylase isoenzymes are present in the circulation: pancreatic type (p-amylase) and salivary type (s-amylase). P-amylase is responsible for approximately 40% of normal serum amylase activity. Initial reports suggested that p-amylase was pancreas specific; however, p-amylase has since been identified in non-pancreatic tissue such as the stomach and duodenum. Therefore, p-amylase is increased in other intra-abdominal diseases, including intestinal obstruction, perforated peptic ulcers and biliary tract disease. S-amylase is increased in tubo-ovarian pathology, alcohol abuse, diabetic ketoacidosis, septic shock, as well as salivary gland lesions. Of note, when our patient was investigated for a ruptured ovarian cyst, the serum amylase concentration was within normal limits.

Both isoenzymes are increased in renal insufficiency. While our patient's renal function was impaired renal insufficiency only results in mild elevations of amylase, usually less than five times the ULN. In addition, hyperamylasaemia can be attributable to macroamylasaemia—an IgA or IgG-bound amylase fraction that cannot be cleared by the renal glomeruli and, subsequently, has an extended half-life in the serum. However, macroamylasaemia is rarely observed in children.² Hyperamylasaemia is also known to occur in patients with acidosis; of note our patient had a profound metabolic acidosis with a pH of 6.9 on admission to ICU. Another important cause of hyperamylasaemia to consider in adolescent females is anorexia nervosa; however, values are generally less than five times the ULN.³

The amylase concentration in this case reached 50 times the ULN and interpretation was complicated by the clinical presentation with abdominal pain. The significant hyperamylasaemia was assumed to be of pancreatic origin, and only when the serum lipase result was returned 5 days later

within reference range was the hyperamylasaemia attributed to soft tissue inflammation in the salivary gland.

There are many salivary gland pathologies known to cause an increase in serum amylase; these include mumps, parotid tumours, trauma, irradiation and obstruction of the salivary duct. However, the serum amylase activity is often not as high as in our case; Howieson *et al*⁴ report a case of parotitis in which the serum amylase peaked at 1477 U/litre.

Had lipase been measured earlier in this case there would have been less concern regarding pancreatitis. Serum lipase offers a superior sensitivity and specificity for the diagnosis of acute pancreatitis; at a cut off of 600 U/litre most studies have reported specificities greater than 95% and sensitivities of 55–100%.⁵ Of note, lipase has a longer half-life than amylase so persists in the circulation after the onset of pancreatitis. For these reasons, the UK guidelines for the management of acute pancreatitis published in 2005 state lipase as the preferred test.⁵ However, assays for lipase are not routinely available in all laboratories because of analytical problems and a lack of consensus on appropriate methodology. Amylase methods specific for p-amylase are available and used by some laboratories.

In summary, our case serves to remind clinicians to consider non-pancreatic causes of hyperamylasaemia. It is important that clinicians consult with biochemistry laboratory staff to review the complete clinical presentation.

Learning points

- ▶ Consider non-pancreatic causes of hyperamylasaemia when appropriate.
- ▶ Interpret biochemistry test results with knowledge of the complete clinical presentation.
- ▶ Consultation with laboratory staff to review unexpected findings or difficult diagnoses can help with result interpretation.

Competing interests None.

Patient consent Obtained.

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