Unusual association of diseases/symptoms

Tramadol poisoning with hyperamylasemia

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Summary

The usual reason for measuring serum amylase level is to confirm or exclude the diagnosis of pancreatitis. However, increases in serum amylase levels can occur in conditions other than pancreatitis and many of those conditions present with acute abdominal pain. In the case presented here, an unconscious patient developed a very high serum total amylase level, which was most likely due to hypoxemia and lactic acidosis secondary to an overdose of Tramadol (Nobligan) tablets. The patient was treated in the intensive care unit and had an uneventful recovery. Many diseases can cause acute elevation of serum amylase level. In lactic acidosis, the hyperamylasemia typically results from the presence of excessive salivary-type isoamylase. Therefore, isoamylase enzyme analysis is of great clinical value in the differential diagnosis of hyperamylasemia, especially in cases with concurrent lactic acidosis.

BACKGROUND

The association between pancreatitis and increase in serum amylase levels is deeply ingrained in physicians' thinking, although very high total serum amylase levels can occur with no signs of pancreatic or salivary gland disease.¹ Many patients are erroneously labelled as having pancreatitis

despite the absence of clinical features to support this diagnosis.²

We describe a case where an unconscious patient presented with extensive hyperamylasemia without pancreatitis after intoxication with Tramadol. To our knowledge, no such case has been described before.

Figure 1 CT scan showing a normal pancreas.

CASE PRESENTATION

A 21-year-old woman was brought unconscious to the emergency department. The patient was found short of breath in her bathroom. Last contact with her was 5 h before admission.

INVESTIGATIONS

Clinically, the patient was cyanotic, had a Glasgow Coma Scale score of 10, she was hypothermic with a core temperature of 34 °C, her blood pressure was 120/70 mm Hg and her pulse rate was 140–150/min and irregular. No signs of trauma were observed. The pupils were normal. ECG showed atrial fibrillation. Arterial blood gas analysis showed serum lactate 13.3 mmol/litre, blood glucose 3.3 mmol/litre, PaCO₂ 9.37 kPa, PaO₂ 6.3 kPa and pH 6.92. Routine screening blood investigations showed that serum total amylase was 4338 U/litre, lactate dehydrogenase 519 U/litre, alanine aminotransferase 137 U/litre, aspartate aminotransferase 67 U/litre, creatinine 147 µmol/litre, white blood cells 14.7 billions/litre and normal C reactive protein. Resuscitation was initiated in the emergency department and the patient was then transferred to the intensive care unit. An initial CT scan of the head, thorax and abdomen showed severe bilateral lung atelectasis, congestion of liver veins, liver oedema, a few millilitres of intraperitoneal fluid and a normal pancreas (see figure 1). The patient responded to supportive treatment with relatively fast recovery. She complained twice about vague mild abdominal pain, but the abdomen was soft without tenderness.

The patient's old hospital chart revealed that she had been admitted two times before because of paracetamol poisoning. However, blood analysis for paracetamol was negative. Serological tests for several viruses showed no evidence of recent infection. Three days after admission the patient disclosed that she had taken about 75 capsules of Tramadol 50 mg (Nobligan; Grünenthal GmbH, Aachen, Germany), which were prescribed to her father. The patient had no history of abdominal pain before the incident and she had no history of gallbladder stones or alcohol abuse.

DIFFERENTIAL DIAGNOSIS

Acute pancreatitis; opioid poisoning.

TREATMENT

Supportive treatment.

OUTCOME AND FOLLOW-UP

The patient had an uneventful recovery. Serum total amylase level decreased to 287 U/litre on the 5th day after admission when she left the intensive care unit and she was dismissed from hospital the next day.

DISCUSSION

The interpretation of abnormally high serum amylase activity is not always straightforward. The usual reason for measuring serum amylase level is to confirm or exclude the

diagnosis of pancreatitis.³ Acute pancreatitis was unlikely in this patient who had only discrete abdominal pain and no radiological changes of the pancreas.⁴ Thus, the Atlanta criteria for diagnosing acute pancreatitis were not fulfilled. Moreover, the patient had no history of alcohol abuse or gallstones.

However, very high serum total amylase levels may also occur in patients with acidosis. In lactic acidosis, the hyperamylasemia typically results from the presence of excessive salivary-type isoamylase.³ It has been reported that acute hypoxaemia may alone or in combination with other factors raise serum total amylase level possibly through ischaemic injury to the pancreas or salivary glands.⁵ Tissue hypoxia, according to this hypothesis, produces hyperpermeability of cell membranes, allowing intracellular amylase to leak out, resulting in high serum total amylase levels.⁶ This might be the mechanism producing hyperamylasemia in shock,⁷ carbon monoxide poisoning,⁶ trauma⁸ and open heart surgery.⁹ Experimental studies suggest that vascular disturbance alone or in conjunction with pancreatic duct obstruction can lead to elevation of serum amylase.¹⁰ Thus, in our case, the very high level of serum total amylase was most likely due to hypoxaemia and lactic acidosis. This seems to be in accordance with the patient's fast recovery where the serum total amylase levels were gradually falling as the acidosis was corrected. Such correlation has been described in the literature where the lower the level of consciousness and the greater the degree of acidosis, the higher the level of amylase.⁶

It has been mentioned that morphine and codeine can cause hyperamylasemia in the absence of pancreatic or salivary gland disease, which might be due to spasm of the sphincter of Oddi, and, subsequently, elevation of pancreatic isoamylase.^{5 11–13} According to the product description sheet for Tramadol, an increase in liver enzymes has been reported in a few isolated cases. Pancreatitis is not mentioned as a side effect or a sign of toxicity.¹⁴ Anyhow, the elevation of amylase and liver enzymes in opioid overdoses is unlikely to be more than 10 times the upper limit of normal, and this elevation is usually associated with CT scan verified pancreatitis.^{11–13}

Kameya *et al* analysed 91 hyperamylasemic sera and traced the patients' records finding that more than half of the patients had a salivary-type isoamylase.⁷ The association between hyperamylasemia and non-pancreatic abdominal pain in patients visiting the emergency room was also reported in other studies.^{15 16} Isoamylase analysis can be of value in differentiating acute abdominal pain. The pancreatic isoamylase (P type) arises only from the pancreas, while salivary isoamylase (S type) is secreted by many different tissues.⁷ Furthermore, the ratio of P type to S type can also be used as a diagnostic tool. A study in patients in the intensive care unit showed that 51% had hyperamylasemia. When isoamylase analysis was done, it showed that the P/S ratio was high in those who had a disorder related to the pancreas, low in patients with extra-pancreatic disorders and normal in patients with renal failure.¹⁰

Learning points

- ▶ Increases in serum total amylase levels most commonly, but not always, signify pancreatitis.
- ▶ Many patients are erroneously labelled as having pancreatitis despite the absence of clinical features to support this diagnosis.
- ▶ Hyperamylasemia can occur due to hypoxaemia and lactic acidosis and it is usually the salivary amylase that increases.
- ▶ Isoamylase enzyme analysis is recommended for diagnosing conditions other than pancreatitis as a cause of hyperamylasemia.

Competing interests None.

Patient consent Obtained.

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