Hypercalcaemia and abdominal pain

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A previously fit 75-year-old woman presented to Accident and Emergency with a 12- hour history of constant upper abdominal pain. Clinical examination revealed pallor but no jaundice and guarding in the epigastrium. Her biochemical results were serum amylase 2878 IU/l (normal <90), bilirubin 33 μmol/l (3–20), alkaline phosphatase 42 IU/l (30–150), aspartate transaminase 354 IU/l (10–50), albumin 38 g/l (35–50), calcium 2.85 mmol/l (2.2–2.6).

Questions

1 What is your differential diagnosis for the abdominal pain?
2 Comment on the relationship between the serum calcium and amylase levels.
3 What further investigations would you request?
4 How would you further investigate and manage the hypercalcaemia if it were due to primary hyperparathyroidism?

Features of hypercalcaemia

- Hypercalcaemia
- Polyuria
- Polydipsia
- Fatigue
- Weakness
- Numbness
- Tingling

Diagnostic tests

- Serum calcium, phosphate, albumin
- 25(OH)D, PTH
- Uric acid
- Urinalysis
- FBC
- Liver function tests
- Alkaline phosphatase, amylase

Management

- Diet: low calcium, low phosphorus
- Vitamin D, calcitriol
- Bisphosphonates
- Dialysis
- Surgery: parathyroidectomy

References

Answers

QUESTION 1

The serum amylase is markedly elevated, favouring a diagnosis of acute pancreatitis. Elevation of the bilirubin and alkaline phosphatase are suggestive of obstructive jaundice and should lead you to consider an obstruction of the common bile duct leading to pancreatitis. Whilst hypercalcaemia is a recognised cause of non-specific abdominal pain and even peptic ulceration (bones, stones, psychic moans and abdominal groans), the magnitude of the serum amylase indicates acute pancreatitis.

QUESTION 2

Hypercalcaemia has been proposed by many authors to be a cause of acute pancreatitis and this relationship is now quoted in many established textbooks. Historical literature reported a higher incidence of acute pancreatitis amongst patients diagnosed with primary hyperparathyroidism compared with a normal hospital population, but more recent literature has not observed this increased incidence casting doubts on any association. Acute pancreatitis is a recognised complication following coronary artery by-pass surgery and the administration of calcium chloride has been observed to be the single most reliable predictor for the development of pancreatitis in a dose-related manner. However, this may just be an epiphenomenon, perhaps related to hypotension-induced pancreatic injury. At present, the association between hyperparathyroidism and acute pancreatitis is unproved. Hypocalcaemia may also be associated with acute pancreatitis. Favoured mechanisms of true hypocalcaemia include calcium deposition in necrotic adipose tissue, cleavage of parathyroid hormone by pancreatic enzymes and a shift in extracellular and intracellular calcium concentration.

QUESTION 3

Recommended further investigations are listed in box 1.

QUESTION 4

Adhere to the general principles of endocrine surgery (box 2).

A diagnosis of acute pancreatitis was confirmed by computed tomography scan of the abdomen. Abdominal ultrasound scan did not reveal gallstones, although the distal common bile duct was mildly dilated to 9.5 mm. The patient was administered analgesia and intravenous fluids and the pancreatitis resolved. A subsequent endoscopic retrograde cholangiopancreatography showed a normal papilla but cannulation of the duct failed. Primary hyperparathyroidism was confirmed by simultaneous hypercalcaemia and an elevated parathyroid hormone. On neck exploration, a solitary 800-mg adenoma was excised from the right superior parathyroid gland. The postoperative calcium levels immediately returned to normal. Six months later the patient remains well with a normal serum calcium and no further attacks of acute pancreatitis.

Final diagnosis

Primary hyperparathyroidism, caused by a solitary adenoma, leading to pancreatitis.

Keywords: adenoma; pancreatitis; hypercalcaemia; hyperparathyroidism

Further investigations

- measurement of prognostic indicators (eg, Glasgow Score)
  on admission: white cell count >18 x 10^9/l; blood glucose >12 mmol/l, lactate dehydrogenase >400 IU/l, aspartate transaminase >240 IU/l during first 48 h: PaO_2 8.0 kPa, albumin <32 g/l, white cell count >15 x 10^9/l, aspartate transaminase >100 IU/l, lactate dehydrogenase >600 IU/l, blood glucose >10 mmol/l, plasma urea >16 mmol/l
  - chest X-ray, particularly if the arterial blood gas results are deranged
  - abdominal ultrasound scan to look for gallbladder stones and cholelithiasis, to examine the appearance of the pancreas and liver, and to measure the diameter of the extrahepatic bile ducts
  - measurement of parathyroid hormone to determine the cause of hypercalcaemia

Box 1

Investigations and management

- confirm the diagnosis: simultaneous hypercalcaemia and inappropriate level of parathyroid hormone
- render the patient safe: intravenous fluids when calcium exceeds 3.0 mmol/l, and bisphosphonates when calcium exceeds 3.5 mmol/l
- consider localisation: not indicated when primary neck exploration performed by an experienced endocrine surgeon
- is surgery indicated? While there is debate as to whether peptic ulcer and acute pancreatitis are indications for parathyroidectomy, a calcium in excess of 2.95 mmol/l is an indication
- what operation? Excise adenomas and discuss with the patient the merits of total or subtotal parathyroidectomy in the presence of multiglandular disease (hyperplasia)

Box 2