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Dysphagia and hypercalcaemia

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A 68-year-old man presented with a 3-month history of progressive dysphagia, anorexia, weight loss, fatigue and malaise. Two years previously, he had received palliative radiotherapy for squamous cell carcinoma of the right bronchus. There was no medical history of gastrointestinal disease and, apart from difficulty swallowing, the patient did not complain of any other gastrointestinal symptoms, urinary symptoms, or visual disturbance. On examination, the patient was alert, but cachectic. There were no signs of cognitive impairment. There was no palpable lymphadenopathy or other mass in the neck. Examination of the mouth and pharynx revealed no abnormalities. Respiratory examination revealed collapse of the right lower lobe. Abdominal examination revealed a hard, irregular, non-tender, non-pulsatile liver edge, palpable 4 cm below the right costal margin. There were no signs of chronic liver disease. Rectal, cardiovascular and neurological examinations were normal. Investigations showed haemoglobin 10.3 g/dl, mean corpuscular volume 78.2 fl, total white blood cell count 8.45×10^9/l (normal differential count) and erythrocyte sedimentation rate 91 mm in the first hour. Renal and thyroid function were normal. Random blood glucose was 6.3 mmol/l. Alkaline phosphatase 487 IU/l (normal range 70-250 IU/l), serum calcium 3.71 mmol/l, serum phosphate 1.17 mmol/l (0.75-1.40 mmol/l) and serum albumin 25 g/l (34-48 g/l). Corrected serum calcium was 4.01 mmol/l (2.22-2.56 mmol/l). Other liver function tests were normal. Serum parathyroid hormone, as measured by radioimmunoassay, was 80 ng/l (< 100 ng/l) and angiotensin-converting enzyme levels were normal. Chest X-ray confirmed collapse of the right lower lobe, due to a carcinoma obstructing the right bronchus. Abdominal ultrasound showed multiple small echogenic lesions throughout the liver, consistent with metastatic deposits from the bronchial carcinoma. An electrocardiogram was normal. An oesophago-gastro-duodenoscopy was normal. In particular, there was no evidence of extrinsic oesophageal compression or oesophageal infiltration by the bronchial carcinoma.

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Questions

1 What is the cause of dysphagia?
2 What other clinical features may be present?

Answers

QUESTION 1

The absence of a mechanical obstruction suggests a neuromuscular cause for dysphagia. In this patient, the cause of dysphagia was hypercalcaemia. He was treated with intravenous normal saline (3 l/24 h) and 30 mg of intravenous pamidronate disodium. Two days later, corrected serum calcium had fallen to 3.22 mmol/l. Five days after admission, his swallowing began to improve and on day six, corrected serum calcium was 2.62 mmol/l. His serum calcium normalised on day eight, (2.48 mmol/l), and on day nine he was able to swallow normally.

QUESTION 2

The other clinical features of hypercalcaemia are given in the box.

Clinical features of hypercalcaemia

General
- fatigue
- weight loss
- muscular weakness
- malaise

Gastrointestinal
- anorexia
- nausea
- vomiting
- dysphagia
- constipation
- dyspepsia
- peptic ulceration
- pancreatitis

Cardiological
- short QT interval on ECG
- cardiac arrhythmias
- hypertension
- vascular calcification

Renal
- renal calculi
- nephrocalcinosis
- polyuria
- dehydration
- renal failure

Psychiatric
- drowsiness
- impaired concentration
- confusion
- psychosis
- depression
- personality changes
- coma

Ophthalmological
- corneal calcification

Discussion

Hypercalcaemia has several recognised effects on the gastrointestinal system, but dysphagia has rarely been reported.[1] Our patient had hypercalcaemia due to metastatic carcinoma of the bronchus. Carcinoma of the bronchus can cause dysphagia due to extrinsic compression or malignant invasion of the oesophagus, but, in this case, no such pathology was found. The rapid improvement in our patient's dysphagia following normalisation of serum calcium levels suggests a causal relationship.

Calcium ions are involved in neuromuscular transmission and muscular contractions. At the neuromuscular junction, release of acetylcholine is stimulated by the rapid influx of calcium ions into the synapse. At the muscular level, rises in intracellular calcium levels stimulate muscular contractions. This occurs in all muscle types. In skeletal muscle, rises in intracellular calcium stimulate interaction between actin and myosin, by removing the inhibitory influence of the troponin–tropomyosin complex. In smooth muscle, calcium ions bind to calmodulin which, via activation of a protein kinase, phosphorylates myosin. This phosphorylation is a pre-requisite for activation of the actin–myosin complex, which leads to muscular contraction. The contractile process of cardiac muscle is similar to that of skeletal muscle.

When serum calcium levels fall, tetany is a recognised sign. This reflects hyperexcitability of the nervous system. This occurs because, as calcium levels fall, neuronal membranes become increasingly permeable to sodium ions, allowing easier propagation of action potentials. Conversely, hypercalcaemia leads to depression of the nervous system. In the gastrointestinal system, this leads to reduced contractility of smooth muscle, which may explain the pathogenesis of dysphagia in patients with hypercalcaemia.

It is important to remember that the oesophagus consists of both skeletal muscle (upper third) and smooth muscle (lower two-thirds). Smooth muscle contains more calcium-dependent channels than skeletal muscle. Dysphagia, therefore, probably results from reduced smooth muscle contractions in the lower two-thirds of the oesophagus. Although the mechanism may not be fully understood, dysphagia should be regarded as a further symptom of hypercalcaemia.

Final diagnosis

Neuromuscular dysphagia due to hypercalcaemia resulting from metastatic carcinoma of the bronchus.

Keywords: hypercalcaemia; dysphagia

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A homesick student

G V McDonnell, T F G Esmonde

A 20-year-old, right-handed female student presented to a neurology clinic having developed depressive symptoms and become withdrawn. Her problems were initially attributed to homesickness. Over the next few months her condition gradually deteriorated. She developed drooling of saliva and retching and her speech became slurred. Her handwriting deteriorated and she was unsteady on her feet. There was urgency of micturition. These various symptoms had resulted in referral to ear, nose and throat and psychiatric services. A computed tomography (CT) scan of brain had been normal.

When first seen at the neurology clinic she was euphoric and mildly dysarthric with drooling. External appearances of the eyes were as shown in figure 1, funduscopy and eye movements being normal. There were dyskinetic movements of all four limbs with dystonic postures of the arms in flexion and adduction. There was normal power in all limbs with symmetrical reflexes. The left plantar response was extensor. She had mildly impaired concentration abilities but orientation and short-term recall appeared normal. There was a reduction in spontaneous speech output. Magnetic resonance imaging (MRI) of the brain was performed (figure 2). Full blood picture, renal function and liver function tests were all normal.

Figure 1 Corneal photograph of right eye

Questions

1 What does the corneal photograph show and what diagnosis does this suggest?
2 What biochemical tests would confirm the diagnosis?
3 What do the MRI scans show?
4 How would you treat this patient?
5 How should her family be managed?

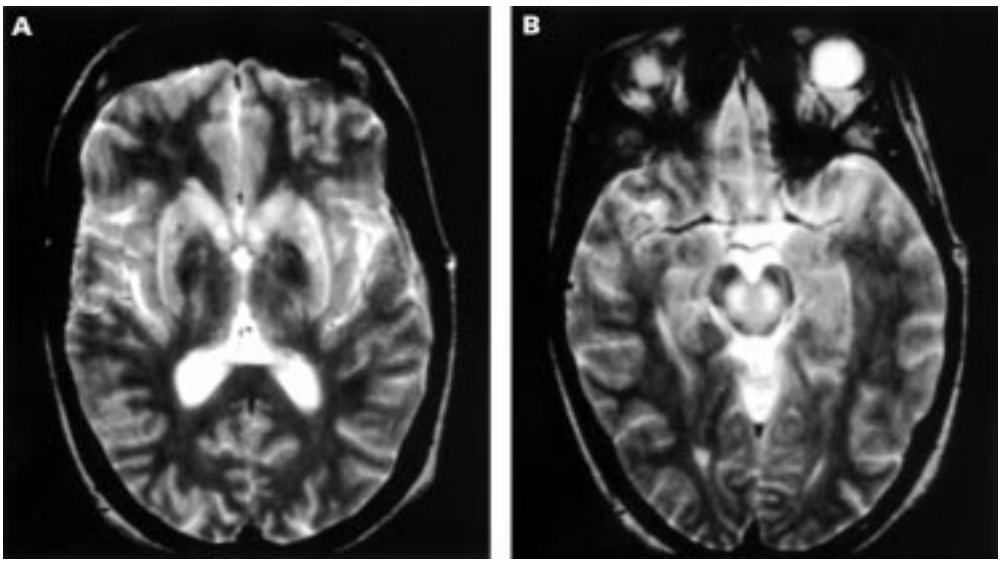

Figure 2 MRI scans of brain, T2-weighted images (TR 4000 ms, TE 76 ms)

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