Unusual association of diseases/symptoms

A rare and life-threatening cause of pseudo-obstruction in two surgical patients

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Summary

We describe two patients who presented with non-mechanical bowel obstruction as a consequence of an underlying, undiagnosed phaeochromocytoma. The first patient was referred by his general practitioner with signs and symptoms of small bowel obstruction on a background of frequent constipation. An abdominal scan revealed an adrenal tumour (subsequently found to be a phaeochromocytoma) but no structural cause for obstruction. Treatment of the phaeochromocytoma was associated with prompt restoration of bowel function.

The second patient was transferred to the intensive care unit on the 8th postoperative day following an elective hip joint replacement. Signs and symptoms of bowel obstruction together with labile blood pressure and progressive lactic acidosis prompted admission to the intensive treatment unit. An abdominal scan identified an infiltrative adrenal tumour but no mechanical cause for bowel obstruction. Histology confirmed a malignant phaeochromocytoma.

Bowel obstruction as the presenting symptom of phaeochromocytoma is well described but rarely identified.

BACKGROUND

These case reports are being published because:

- ▶ The association between phaeochromocytoma and pseudo-obstruction is poorly recognised.
- ▶ Medication and procedures that surgical patients commonly receive may precipitate a phaeochromocytoma crisis.
- ▶ Many cases of phaeochromocytoma remain undiagnosed with 40% of diagnoses made at postmortem.¹
- ▶ The consequences of missing this diagnosis can be fatal; however, appropriate treatment is usually curative as 90% of tumours are benign.

Case number 1

A man aged 68 years was referred by his general practitioner with abdominal pain, distension and vomiting. He had not opened his bowels in 7 days. His medical history included hypertension (controlled by several antihypertensives), anxiety attacks and peripheral vascular disease (PVD). Systems enquiry revealed a tendency to constipation, headache, palpitations and heavy sweating. Examination confirmed a soft but distended abdomen with reduced bowel sounds and the abdominal x-ray confirmed dilated loops of small bowel consistent with obstruction (figure 1A). The patient was managed with intravenous

Figure 1 (A) X-ray: suggestive of small bowel obstruction (B) CT: right adrenal tumour.

Figure 2 (A) X-ray: suggestive of small bowel obstruction (B) CT: infiltrative left adrenal tumour.

fluids and a nasogastric tube and his condition stabilised. A CT was arranged and this revealed a unilateral 10 cm right adrenal tumour (figure 1B) but no structural cause for the bowel obstruction. Adrenal biochemical screen was requested and his urine catecholamines were diagnostic of phaeochromocytoma. α -Blockers were commenced and within hours his bowel symptoms resolved. A cardioselective β -blocker was cautiously added-in several days later without exacerbation of his PVD. He remained an inpatient and underwent uneventful resection of the phaeochromocytoma. Histology confirmed complete removal of a benign encapsulated tumour. Thereafter, his bowel habit normalised, anxiety attacks, headaches and palpitations resolved, and his blood pressure became controlled on a single agent. He remains in biochemical remission 7 years on from his surgery.

Case number 2

A woman aged 70 years had a medical history of tablet controlled type 2 diabetes and hypertension and had also been troubled with bouts of constipation in recent years. She had been admitted for an elective hip replacement, performed under spinal anaesthetic. Her postoperative course was turbulent, culminating in an urgent admission to the intensive care unit on the 8th postoperative day. Initial symptoms of concern were fever, supraventricular tachycardias and hypertension, for which she was started on broad spectrum antibiotics and a β -blocker. Her condition worsened and she developed signs of bowel obstruction, namely abdominal swelling, discomfort, vomiting and constipation (abdominal x-ray; figure 2A). She continued to deteriorate despite intravenous fluids and a nasogastric tube insertion, becoming progressively more peripherally cyanosed despite of significant hypertension (200/100 mm Hg). Thereafter, her respiratory rate climbed in compensation for a progressive lactic acidosis (lactate >14), urine output fell, and she was transferred urgently to the intensive treatment unit. An urgent CT scan failed to identify a cause for the bowel obstruction but did reveal a large left adrenal tumour that infiltrated the adrenal vein, however there were no distant metastases (figure 2B). β -Blockers were stopped and an urgent adrenal biochemical screen was ordered. This was followed by the initiation of intravenous α -blockers for a

presumed phaeochromocytoma crisis. Urine catecholamines were consistent with a diagnosis of a phaeochromocytoma and an urgent laparotomy was arranged for resection of the tumour. At laparotomy ischaemic bowel was also encountered and this was resected together with the tumour. Unfortunately, the patient's condition deteriorated, progressing to disseminated intravascular coagulation and she died on her 6th intensive treatment unit day. Histology confirmed an infiltrative malignant phaeochromocytoma.

BIOCHEMISTRY RESULTS AT PRESENTATION WITH PSEUDO-OBSTRUCTION

Case 1

- ▶ Sodium – 134 mmol/l (135–145)
- ▶ Potassium – 3.5 mmol/l (3.4–5)
- ▶ Urea – 10.0 mmol/l (2.5–7)
- ▶ Creatinine – 130 μ mol/l (70–120)
- ▶ Magnesium – 0.75 mmol/l (0.7–1.0)
- ▶ Liver function tests – normal
- ▶ Bone profile – normal
- ▶ C reactive protein (CRP) 20 mg/l (<6)
- ▶ Thyroid function test – normal
- ▶ Glucose – 7 mmol/l (3–7.7)
- ▶ Urine volume – 3728 ml/24 h
- ▶ Normetadrenaline – 42.39 μ mol/24 h (<4.0)
- ▶ Metadrenaline – 0.3 μ mol/24 h (<2.0).

Case 2

- ▶ Sodium – 143 mmol/l (135–145)
- ▶ Potassium – 3.6 mmol/l (3.4–5)
- ▶ Urea – 10.0 mmol/l (2.5–7)
- ▶ Creatinine – 125 μ mol/l (70–120)
- ▶ Magnesium – 0.75 mmol/l (0.7–1.07)
- ▶ Albumin – 23 g/l (35–50)
- ▶ Corrected calcium – 2.23 mmol/l (2.2–2.6)
- ▶ Phosphate – 1.64 mmol/l (30–115)
- ▶ Alkaline phosphatase – 119 IU/l (30–115)
- ▶ CRP 18 mg/l (<6)
- ▶ Thyroid function test – normal
- ▶ Glucose – 12 mmol/l (3–7.7)
- ▶ pH – 7.33 (7.35–7.45)

- ▶ $p\text{CO}_2$ – 2 KPa (4.7–6)
- ▶ $p\text{O}_2$ – 35 KPa (11.1–14.4)
- ▶ Standard bicarbonate – 12 mmol/l (22–27)
- ▶ Base excess minus – 18 mmol/l
- ▶ Lactate – 14.5 (0.5–1.6)
- ▶ Urine volume – 1984 ml/24 h
- ▶ Normetadrenaline – 39.34 $\mu\text{mol}/24\text{ h}$ (<4.0)
- ▶ Metadrenaline – 95.23 $\mu\text{mol}/24\text{ h}$ (<2.0)
- ▶ Epinephrine – 15636 $\mu\text{mol}/24\text{ h}$ (15–160)
- ▶ Dopamine – 2982 $\mu\text{mol}/24\text{ h}$ (540–4440).

DIFFERENTIAL DIAGNOSIS FOR AN ILEUS/PSEUDO-OBSTRUCTION

- ▶ Metabolic imbalance: hypokalaemia, hypocalcaemia, hypophosphataemia, hyponatremia
- ▶ Postoperative paralytic ileus (rarely beyond the 5th postoperative day and usually related to abdominal surgery)
- ▶ Drug induced (ie, opiates, anticholinergics)
- ▶ Gastrointestinal autonomic neuropathy, i.e. Diabetes
- ▶ Hypothyroidism
- ▶ Hirschsprung's disease.

OUTCOME AND FOLLOW-UP

The man described remains disease free 7 years on from his surgery. His constipation and panic attacks have resolved and his blood pressure is now controlled on a single agent.

DISCUSSION

Phaeochromocytoma is a tumour that produces supra-physiological quantities of catecholamines, either continuously or intermittently. In 90% of cases it originates from the adrenal gland, the remainder being extra-adrenal paragangliomas. Between 10–20% of cases occur as a consequence of specific germ-line mutations which are associated with several recognised conditions (including multiple endocrine neoplasia type 2, Von Hippel Lindau syndrome and Neurofibromatosis). Ileus or pseudo-obstruction is an unusual but recognised presentation of phaeochromocytoma.^{2–4} Typical symptoms which may be revealed in the history of such patients include anxiety attacks, headache, palpitations and heavy sweating and the patient commonly has hypertension. Case 1 displayed all of these symptoms.

Phaeochromocytoma may precipitate non-mechanical bowel obstruction or paralytic ileus in response to the excessive sympathetic stimulation of gut viscera. Parasympathetic innervation drives peristalsis and relaxes gut sphincters, whereas sympathetic stimulation has the reverse effect⁵ while simultaneously vasoconstricting the mesenteric vessels. At lower levels this sympathetic drive can result in constipation (reported in 5–13% of phaeochromocytoma cases in one series⁶), whereas excessive sympathetic stimulation can paralyse the bowel resulting in pseudo-obstruction/ paralytic ileus or, in extreme cases, megacolon.⁴ Bowel ischaemia and necrosis (as seen in case 2) have been described in association with phaeochromocytoma.⁷ α -Adrenoceptor blockers have been known to promptly restore peristalsis and bowel function,^{8–9} as was seen in case 1. An association between the size and metabolic activity of phaeochromocytomas and their tendency to cause paralytic ileus and certainly megacolon has been proposed.^{4–10}

Many factors can precipitate a catecholamine surge from phaeochromocytoma in untreated patients. Those relevant to this case include morphine based analgesics and metoclopramide,¹¹ radiological contrast agents,¹² intubation/ anaesthetic agents^{13–14} (in the event of surgery and anaesthesia being required) and, of course, direct pressure or manipulation of the tumour.¹⁵

Phaeochromocytoma crisis is a life-threatening situation with a high mortality. Death from crisis may occur through several mechanisms including fatal cardiac arrhythmias, end organ complications of acute malignant hypertension (ie, myocardial infarction, cardiogenic shock, cerebral haemorrhage) and haemodynamic collapse.

The medical management of phaeochromocytoma involves the careful introduction and up-titration of α -blockers to achieve optimal α -blockade (traditionally taken to be postural hypotension and nasal stuffiness). This must be achieved before β -blockers are added-in for control of potential tachyarrhythmias. β -2 Receptor stimulation mediates vasodilation in the systemic vasculature, whereas α -adrenoceptors cause vasoconstriction. Therefore, the introduction of β -blockers alone can precipitate an acute rise in blood pressure which may progress to malignant hypertension and its adverse consequences.¹⁶ Although case 2 received a low dose of a β -blocker to control her recent tachyarrhythmias, this may have contributed to her progressive clinical deterioration on the ward. Although medical treatment allows control of the symptoms of phaeochromocytoma in the short term, cure is achieved from surgical resection of the tumour.

Our case presentations draw attention to the bowel symptoms and their mechanisms that can occur in phaeochromocytoma, namely pseudo-obstruction and paralytic ileus. The report illustrates the need to consider associated symptoms that may draw attention to the possibility of an underlying phaeochromocytoma in such patients. Our cases demonstrate the successful outcome that can be achieved with appropriate medical and surgical intervention, and the tragedy that may occur as a consequence of a missed or delayed diagnosis.

Learning points

- ▶ Pseudo-obstruction and paralytic ileus can occur as a consequence of an underlying phaeochromocytoma.
- ▶ Vigilance to atypical symptoms is important as many cases of phaeochromocytoma remain undiagnosed.
- ▶ Appropriate medical and surgical treatment of phaeochromocytoma will have a successful outcome in most cases.

Competing interests None.

Patient consent Obtained.

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de Lloyd AC, Munigoti S, Davies JS, Scott-Coombes D. A rare and life-threatening cause of pseudo-obstruction in two surgical patients. *BMJ Case Reports* 2010; 10.1136/bcr.04.2010.2882, date of publication

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