Intestinal ischaemia associated with phaeochromocytoma

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Summary: The present case report describes a patient with an adrenal phaeochromocytoma who presented with infarction of the small intestine. The clinical features, diagnosis and treatment of this case are described. Despite excision of the tumour and necrotic intestine, this patient died in the postoperative period from overwhelming sepsis and multi-organ failure. Special reference is made to the delayed effects of established intestinal ischaemia on immune function and it is suggested that this was major contributory factor to the fatal outcome in the present case. The onset of gastro-intestinal symptoms in patients with phaeochromocytoma should suggest the possibility of imminent gut ischaemia and indicate the necessity for prompt excision of the tumour.

Introduction

Phaeochromocytoma is an uncommon tumour which usually produces paroxysmal episodes of hypertension, headache, sweating and palpitations.^{1,2} Other presentations are well recognized and the clinical picture may simulate diabetes mellitus, cardiac disease and hyperthyroidism.³ By contrast, major gastrointestinal manifestations have only rarely been reported and their association with phaeochromocytoma may be overlooked. The present report describes a patient with phaeochromocytoma who developed the unusual complication of small intestinal ischaemia.

Case report

A 44 year old Caucasian woman was admitted to a referring hospital with an 8-day history of febrile illness, an erythematous rash, painful cold limbs and vomiting. In addition, she had a one month history of intermittent abdominal pain and 6 years previously she had seen a psychologist for tension headaches which had been experienced regularly ever since. Examination revealed an erythematous rash on her face, neck and trunk and central cyanosis. Her blood pressure was 190/110 mmHg, pulse rate 120/minute and she had evidence of severe vasospasm in her hands and feet with impalpable foot pulses. Initial investigation revealed haemoglobin 16.1 g/dl, white cell count $12 \times 10^9/l$, platelets $326 \times 10^9/l$, serum sodium 133 mmol/l, serum potassium 5 mmol/l, blood urea 10.2 mmol/l, blood glucose 10.2 mmol/l and serum creatine kinase 2098 IU/l. Chest X-ray was normal but electrocardiogram showed a sinus tachycardia with T

wave inversion in the anterior chest leads. A provisional diagnosis of a collagen vascular disorder with severe acute vasospasm was made and treatment commenced with nifedipine, intravenous fluids and naftidrofuryl oxalate (Praxilene) with some improvement in her peripheral circulation. Over the course of the next 4 days she developed increasing abdominal pain and dyspnoea. Examination showed signs of peritoneal irritation in the right iliac fossa and pulmonary oedema. There was diffuse shadowing of both lung fields on chest X-ray and small bowel dilatation with multiple fluid levels was apparent on plain abdominal X-ray. Ultrasound examination was performed on the 5th day and revealed a large right sided suprarenal mass suspicious of a phaeochromocytoma.

After further deterioration she was transferred to the Middlesex Hospital. On arrival she was critically ill with the signs of pulmonary oedema and generalized peritonitis. A computed tomographic scan confirmed the presence of a suprarenal mass with appearances typical of a phaeochromocytoma (Figure 1). Urinary vanilmandelic acid (VMA) excretion was grossly elevated at 960 mmol/24 hours (normal range less than 25 mmol/24 hours).

Laparotomy was performed 12 hours after admission. There was patchy gangrene of the distal third of the small intestine which was resected and the remaining bowel ends exteriorized. A 9 cm diameter suprarenal mass was excised with minimal blood loss. In the immediate postoperative period intravenous infusions of adrenaline, noradrenaline and dobutamine hydrochloride were required to maintain cardiac output but these agents were discontinued after 48 hours when she was haemodynamically stable. On the 5th post-operative day she suddenly deteriorated and developed a *Pseudomonas* septicaemia complicated by

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Figure 1 A contrast enhanced CT scan showing a well defined mass with numerous non-enhancing spaces of fluid density. The mass is contiguous to the diaphragm and displaces the inferior vena cava anteriorly (arrow). The site and internal characteristics of this mass are typical of an adrenal pheochromocytoma.

the adult respiratory distress syndrome and renal failure. Despite further intensive therapy which included ventilation, inotropic support, haemofiltration and intravenous azlocillin she died on the 10th postoperative day.

Examination of the surgical specimen revealed a soft encapsulated tumour $9 \times 9 \times 8$ cm and weighing 192 g which on histological examination had the features of a pheochromocytoma. The resected small intestine displayed transmural necrosis with recent fibrin microthrombi in small veins and venules but no degenerative vascular lesions or arteritis. At post-mortem there was no significant intra-abdominal pathology and microscopic examination revealed no microinfarction of any other vital organs.

Discussion

Several major reviews^{1,2,4} and standard texts⁵ either make little reference to or fail to mention intestinal ischaemia as part of the clinical spectrum of pheochromocytoma. Sporadic case reports have drawn attention to this unusual association and presentations include gastrointestinal tract bleeding,⁶ enterocolitis^{7,8} and, as in our patient, infarction of the small intestine.^{9,10} Cruz *et al.*¹¹ suggested that ischaemic complications occur more frequently with tumours weighing more than 70 grams which release

massive amounts of catecholamines into the circulation. This may have been a predisposing factor to the development of ischaemia in the present case and may also explain the low incidence of this complication in many reported series.

The cause of ischaemia may rarely be traced to structural lesions of small mesenteric vessels. Brown *et al.*¹² demonstrated fibrinoid necrosis of intramural arterioles in 2 patients who presented with ischaemic perforation of the small bowel. These authors postulated that these vascular lesions are mediated by the systemic hypertension associated with pheochromocytoma. This hypothesis is supported by the observation that fibrinoid necrosis of gut arterioles may be present in 9–15% of patients dying from severe systemic hypertension¹³ and that similar vascular lesions can develop in response to the paradoxical hypertension which sometimes follows corrective surgery for coarctation of the aorta.¹⁴ In 5 other reported cases structural vascular lesions have not been demonstrated.^{7–10} The absence of degenerative vascular lesions and arteritis on histological examination of the bowel from the present case are in keeping with these observations. It seems likely that under these circumstances ischaemia is the result of reduced splanchnic blood flow due to profound vasospasm induced by high circulating levels of catecholamines.

It is clear from this and other reports that, despite intensive resuscitation and effective surgery the outcome of small intestinal ischaemia complicating pheochromocytoma is often fatal. Recurrent bowel ischaemia^{8,9,12} and microinfarction of other vital organs due to severe and generalized vasospasm^{9,12} have been recorded as important causes of death. These did not occur in the present patient who died from overwhelming sepsis developing later in the postoperative period. The association between intestinal ischaemia and delayed postoperative sepsis is well recognized but the reasons for it are uncertain. It has recently been recognized that acute intestinal ischaemia causes the leakage of large amounts of lipopolysaccharide and prostaglandins into the circulation in addition to stimulating monocytes to release tumour necrosis factor (TNF).^{15,16} These substances can suppress a variety of immune functions.¹⁷ Furthermore, disruption of the mucosal barrier occurs as the result of ischaemia and facilitates bacterial translocation which provides a potential source of circulating pathogens.¹⁸ Fiddian-Green *et al.*^{19,20} noted that there may be a delay of several days between the ischaemic episode and the onset of sepsis which may represent the time taken for immune dysfunction to develop before translocated or exogenous organisms can establish infection.¹⁷ It seems that intestinal ischaemia has the potential to produce immunodepression and that the effect of this on the natural history of delayed postoperative sepsis is likely to be critical.

In patients undergoing elective excision of phaeochromocytoma the use of alpha blocking agents has been widely advocated as a means of controlling preoperative blood pressure and minimizing blood pressure fluctuations during surgery.² Although similar pharmacological manoeuvres have been encouraged for use in the emergency situation²¹ alpha blockade may cause prolonged hypotension due to widespread vaso-dilatation and depletion of circulating fluid volume as the result of plasma transudation.³ In the present patient who was profoundly fluid-depleted

due to intestinal ischaemia and septicaemia, alpha blockage was therefore felt to be inappropriate.

An improvement in this situation can only be expected if clinicians are aware of the rare association between phaeochromocytoma and intestinal ischaemia. We concur with the opinion of Fee *et al.*⁷ that gastrointestinal symptoms in patients with phaeochromocytoma should suggest the possibility of imminent gut ischaemia and indicate the necessity for prompt excision of the tumour.

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