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A man presenting with limb weakness and electrolyte imbalance

J C Smith, C Meehan, P Lyons, A M Robinson

A 39-year-old man presented with lower limb muscle pains and weakness which had progressed rapidly over the preceding 2 weeks. Immediately prior to hospital admission he was unable to stand unaided. There had been no disturbance of bulbar, sensory or sphincter function and he reported no recent gastrointestinal symptoms. Medical history included colitis, which was quiescent. His only regular medication was olsalazine. On examination, he was normotensive (and remained so throughout his admission). There was no rash. Cardiovascular, respiratory and abdominal examinations were normal. Neurological examination revealed generalised weakness in all four limbs, most marked proximally. Tendon reflexes were preserved. Plantar response was flexor. Examination of cranial nerves was normal.

Laboratory investigations revealed a serum potassium of 1.8 mmol/l. Serum sodium, urea and creatinine were within normal limits. Creatine kinase was 10 719 IU/l. A quadriceps muscle biopsy was performed and the histology is shown in figure 1. Further investigations included an abdominal ultrasound scan, following which computed tomography (CT) of the abdomen was performed (figure 2). A 24-hour urine collection for catecholamines was undertaken (table).

Figure 1 Quadriceps muscle biopsy

Figure 2 CT scan

Royal United Hospital,
Bath, UK
Department of
Medicine
J C Smith
A M Robinson
Department of
Pathology
C Meehan
Department of
Neurology
P Lyons

Correspondence to
Dr Jamie Smith, Research
Fellow, Department of
Endocrinology, Diabetes and
Metabolism, A7 Office,
University Hospital of Wales,
Heath Park, Cardiff CF4
4XN, UK

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Table Levels of free catecholamines (laboratory normal in brackets)

Catecholamine	
Noradrenaline (nmol/24 h)	3328 (<800)
Adrenaline (nmol/24 h)	725 (<100)
Dopamine (nmol/24 h)	>45 000 (<3100)

Questions

- 1 What does the CT scan show?
- 2 What is the likely underlying diagnosis?
- 3 What are the three most common presenting symptoms for this condition?
- 4 What caused the muscular signs and symptoms?

Answers

QUESTION 1

The CT scan (figure 2) shows a large mass (arrow) arising from the region of the right adrenal gland. It has displaced the liver and kidney on that side. The contralateral adrenal is just visible anterior to the left kidney. The appearances are therefore compatible with an adrenal tumour.

QUESTION 2

The 24-hour urinary collection shows significantly elevated levels of noradrenaline, adrenaline and dopamine. These three catecholamines are the dominant secretory products of phaeochromocytomas. In this case, the dopamine levels are grossly elevated and predominate. These biochemical findings by themselves suggest the presence of a phaeochromocytoma which, in view of the CT findings, is likely to have an adrenal origin.

QUESTION 3

Phaeochromocytomas are well known for their diverse clinical presentation and manifestations. The three most common presenting symptoms, which classically occur in intermittent episodes or 'attacks', are headache (60% of cases), sweating (52%) and palpitations (49%).¹ Hypertension is constant in only about 50% of patients, paroxysmal in about 30% and absent in approximately 20%.

QUESTION 4

Generalised muscle weakness associated with a markedly elevated creatine kinase suggests widespread muscle injury. The histology from the muscle biopsy (figure 1) shows scattered myofibre necrosis with no evidence of inflammation or vasculitis. These appearances are consistent with rhabdomyolysis. Muscle damage has been known to occur in association with phaeochromocytoma, with previous reports postulating that ischaemic muscle injury results from catecholamine-mediated vasoconstriction.² However, the direct cause in this case is likely to be hypokalaemia. Marked potassium depletion impairs striated muscle function, causing weakness typically affecting shoulder and pelvic girdle musculature. When hypokalaemia is severe (<2.5 mmol/l) or prolonged, a full blown hypokalaemic myopathy may develop, leading to myositis or frank rhabdomyolysis.³

Discussion

This case illustrates an unusual presentation of a catecholamine-secreting tumour. The patient developed a reversible hypokalaemic myopathy as a direct result of the tumour. This myopathy resolved following the restoration of normokalaemia using potassium supplementation. It is likely that the hypokalaemia arose as a direct result of the tumour. Phaeochromocytomas arise from chromaffin cells which belong to the APUD (amine precursor uptake decarboxylase) series of cells. These cells are capable of co-secreting other peptide hormones whose

Learning points

- clinical manifestations of phaeochromocytoma can be diverse and may reflect the type of predominant catecholamine as well as other peptide hormones potentially secreted by the tumour
- tumours secreting predominantly dopamine often present without hypertension and sometimes cause hypotension
- severe hypokalaemia can cause neuromuscular symptoms and may lead to muscle necrosis and rhabdomyolysis
- high levels of circulating catecholamines can cause hypokalaemia by ionic shift. This phenomenon can also occur after exposure to beta agonists

effects can confuse the diagnosis and contribute to the diverse clinical manifestations seen with phaeochromocytomas. Hypokalaemia could result from the actions of such hormones. Adrenocorticotropin can, for example, be secreted, producing hypercortisolism⁴ and similarly, vasoactive intestinal peptide secretion can cause a syndrome of watery diarrhoea associated with gastrointestinal potassium loss. Catecholamines, particularly adrenaline, can also directly cause hypokalaemia of physiological importance through stimulation of beta 2 receptors causing activation of sodium-potassium-ATPase in skeletal muscle and subsequent ionic shift of potassium.⁵ This is thought to be the mechanism responsible for hypokalaemia occurring during acute myocardial infarction when levels of circulating adrenaline are high.

Another unusual feature of this case was the complete absence of hypertension, despite a tumour producing high levels of catecholamines. The symptoms and signs associated with phaeochromocytoma are largely related to the amount and type of catecholamine synthesised and released by the tumour. Noradrenaline, adrenaline and dopamine each have differing pharmacological effects. Noradrenaline secretion is associated with systolic and diastolic hypertension but also shrinkage of the plasma volume with a resultant rise in the haematocrit and the development of postural hypotension. Adrenaline-secreting tumours stimulate beta-adrenoceptors leading to tachycardia, cardiac arrhythmias and metabolic effects including glycogenolysis and lipolysis. Predominantly dopamine-secreting tumours are characteristically associated with an absence of hypertension and sometimes produce hypotension by counteracting the vasoconstricting effects of noradrenaline, as well as producing vasodilatation in renal and mesenteric vasculature.⁶ These factors are likely to explain the absence of hypertension in this particular case. All clinical and biochemical abnormalities resolved following surgical removal of the tumour.

Final diagnosis

Phaeochromocytoma presenting with hypokalaemic rhabdomyolysis.

Keywords: phaeochromocytoma; hypokalaemia; rhabdomyolysis

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Central cyanosis in a young man

Uma Kumar, Praveen Aggarwal, Rohini Handa, Renu Saxena, Jyoti Prakash Wali

All India Institute of Medical Sciences,
110029 New Delhi,
India
Department of Medicine
U Kumar
P Aggarwal
R Handa
J P Wali
Department of Haematology
R Saxena

Correspondence to
Praveen Aggarwal

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A 25-year-old man presented with bluish discoloration of body, lips and nails since birth. He denied any other significant complaints. General examination revealed presence of central cyanosis with steel-grey complexion of the body. He did not have clubbing of nails. Systemic examination was unremarkable. Investigations showed a haemoglobin of 17.2 g/dl and a normal blood chemistry. The arterial blood gas analysis while the patient was breathing room air revealed a PaO₂ of 100.9 mmHg and an oxygen saturation of 97.8%.

Questions

- 1 What is the probable diagnosis?
- 2 What are the common causes of central cyanosis?
- 3 How would you approach a patient with central cyanosis?
- 4 What is the appropriate management in the present case?