naturally occurring malaria. The mechanism of thrombocytopenia is controversial, but is probably multifactorial. In our patient it might have been due to production of antiplatelet antibody of IgM class.³

Evidence of bleeding without DIC is rare. Beale *et al*³ reported one case of subconjunctival haemorrhage among 17 people with thrombocytopenia, three cases of epistaxis, and one of haematuria, but we believe our report to be the first record of cutaneous purpura in malaria. We should like to emphasise that thrombocytopenia and haemorrhage may occur in malaria without DIC. Controversy over the use of heparin in DIC is rife,⁴ but clearly unequivocal evidence of DIC must be obtained before heparin treatment is started.

¹ Communicable Diseases Report No 34-35. London, Public Health Laboratory Service, 1976.

² Esan, G J F, *Clinics in Haematology*, 1975, 4, (1), 247.

³ Beale, P J, Cormack, J D, and Oldrey, T B N, *British Medical Journal*, 1972, 1, 345.

⁴ Reid, H A, *Lancet*, 1975, 1, 167.

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Glibenclamide and syndrome of inappropriate secretion of antidiuretic hormone

The oral hypoglycaemic drug glibenclamide has been reported to cause a diuresis both in healthy people and in patients with diabetes mellitus.¹ This effect may be due to antagonism to the action of antidiuretic hormone (ADH).² We have used glibenclamide to treat a patient with the syndrome of inappropriate secretion of ADH (SIADH) with the following results.

Case report

A 30-year-old woman with SIADH of unknown aetiology was admitted to the metabolic unit. There was no evidence of intracranial disease, renal disease, chest disease, or neoplasia, and her management had consisted in fluid restriction since the diagnosis was made five years earlier. After a baseline period of three days a 12-hour water deprivation test with measurement of maximum urine osmolality was performed. Next day a four-hour water tolerance test was carried out with a challenge of 1 litre of water, the urine volume and minimum urine osmolality being measured. The patient was then given oral glibenclamide 2.5 mg each morning, the water deprivation and water tolerance tests being repeated on the third and fourth days of treatment, starting two hours after the dose of glibenclamide. The dose was then increased to 5 mg daily and subsequently to 10 mg daily and the procedure repeated. Finally, the investigations were repeated after two days only on 20 mg daily. Plasma osmolality was measured before each water test, and plasma ADH was measured³ during the baseline period and before the water tests two hours after giving the 10-mg and 20-mg doses. During the entire study period the daily intake of sodium, potassium, and fluid remained constant. Plasma glucose was monitored throughout the study.

Plasma ADH was raised during the baseline period at 12.3 ng/l (normal range 4-8 ng/l) and remained raised during the treatment with glibenclamide. In addition there was no significant change in any of the variables measured during treatment compared with the baseline period (figure). In particular, no increase in urine flow was seen, in contrast to previous reports.^{1,2}

Comment

In this patient glibenclamide did not modify the circulating concentration of ADH and did not have a diuretic effect. Our findings suggest that the diuretic effect of glibenclamide may not be through antagonism of ADH or through suppression of ADH secretion. Alternatively, the ADH concentrations in this patient may have been

Absence of significant change in variables measured during treatment with glibenclamide.

Conversion: SI to traditional units—Urine and plasma osmolalities: 1 mmol/kg = 1 mOsm/kg.

too high for antagonism of ADH and consequent diuresis to be apparent.

¹ Moses, A M, Howanitz, J, and Miller, M, *Annals of Internal Medicine*, 1973, 78, 541.

² Rado, J P, Szende, L, and Marosi, J, *Metabolism*, 1974, 23, 1057.

³ Morton, J J, Padfield, P L, and Forsling, M L, *Journal of Endocrinology*, 1975, 65, 411.

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Bronchial carcinoma metastasising to the ischiorectal fossa

Carcinoma of the bronchus is noted for its tendency to metastasise extensively. Nevertheless, it rarely metastasises to muscle and it has never been reported as spreading to fat. We report a case of carcinoma of bronchus which presented with a secondary deposit in the fat and muscle of the ischiorectal fossa.

Case report

A 72-year-old man presented with a two-week history of perianal pain exacerbated by the passage of stool. He had been well, specifically denying any weight loss and respiratory symptoms. He was a heavy smoker and had not been on antibiotics preceeding admission. He was afebrile, with a large

ischio-rectal mass which was not fluctuant. Sigmoidoscopy to 20 cm showed no intrinsic rectal lesion. At exploratory operation the entire ischio-rectal fossa was replaced by woody hard tumour, with surrounding inflammation. No pus was obtained and bacteriological swabs of the mass gave no growth on culture. Histological examinations of biopsy specimens showed fat and muscle infiltrated with poorly differentiated squamous carcinoma consistent with an origin in the bronchus. The chest x-ray film had disclosed an opacity in the right hilum, suggestive of bronchial carcinoma. Subsequent bronchoscopy confirmed the presence of a carcinoma arising from the right bronchus—biopsy specimens showed that it was a squamous-cell carcinoma.

Discussion

In a review of published work we have been unable to find any recorded cases of carcinoma of bronchus spreading to the ischio-rectal fossa, though bronchial carcinoma metastasising to the gluteus maximus and presenting as a gluteal abscess has been reported.¹ Furthermore, a review of 16 394 necropsies (747 cases of bronchial carcinoma) found no evidence of metastasis to the ischio-rectal fossa but noted secondary deposits in the rectum in 2.2% of cases.² The mechanism of spread is uncertain. The tendency of malignant cells to metastasise to areas of trauma or inflammation is well known.³ Possibly a sub-clinical episode of infection in the ischio-rectal fossa occurred, with resultant deposition of tumour cells locally. The histological similarity of biopsies taken and the negative findings at sigmoidoscopy excludes the possibility of two primary tumours.

We are grateful to Mr D Pratt for his comments and for allowing us to report this case.

¹ Ramanathan, T, *British Journal of Diseases of the Chest*, 1973, **67**, 167.

² Berge, T, and Toremalm, N G, *Scandinavian Journal of Respiratory Diseases*, 1975, **56**, 109.

³ Fisher, B, Fisher, E K, and Feduska, N, *Cancer*, 1967, **20**, 23.

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Rebound phenomenon during gradual withdrawal of clonidine

Clonidine is a powerful antihypertensive agent. If long-term treatment is suddenly discontinued it may precipitate a withdrawal crisis, in which sharp increases in blood pressure and urinary and blood catecholamines occur.¹ We investigated the possibility that this syndrome could be prevented by gradual withdrawal of the drug in a patient who had been taking excessive doses of clonidine.

Case report

A 21-year-old man was admitted to hospital for readjustment of his anti-hypertensive treatment. Three years previously essential hypertension had been diagnosed. His blood pressure was 200/110 mm Hg and clonidine treatment was started. Whenever he forgot to take the clonidine he became acutely agitated. He also complained of flushes, and therefore increased the doses of clonidine spontaneously. On admission he was taking 3 mg/day and his blood pressure was 120/80 mm Hg. Since he seemed unreliable and had a history suggestive of repeated withdrawal crises, we decided to start him on a new course of treatment. A careful withdrawal schedule was planned.

Urine was collected for 24-hour measurement of catecholamines (maximum normal values: noradrenaline 0.55 $\mu\text{mol}/24\text{ h}$ (100 $\mu\text{g}/24\text{ h}$); adrenaline 0.12 $\mu\text{mol}/24\text{ h}$ (20 $\mu\text{g}/24\text{ h}$), measured fluorometrically). Supine blood pressure was recorded four times a day. The means of systolic and diastolic pressure were calculated daily. Clonidine dosage was decreased by 0.3 mg for the first five days, and by 0.15 mg for the next 10 days.

During withdrawal blood pressure gradually increased to a maximum mean value on day 14 of 212/126 mm Hg (figure). The maximum value recorded was 242/134 mm Hg, which greatly exceeded the initial pretreatment values. Catecholamine concentrations were low during the first 10 days, but started to rise gradually on day 11, reaching a maximum value of 1 $\mu\text{mol}/24\text{ h}$ (190 $\mu\text{g}/24\text{ h}$) on day 15. When catecholamine concentrations were maximal the patient was anxious and could not sleep.

Mean blood pressure values and urinary catecholamine concentrations during and after gradual withdrawal of clonidine.

Conversion: SI to traditional units—urinary catecholamines (as adrenaline) 1 $\mu\text{mol}/24\text{ h}$ = 183 $\mu\text{g}/24\text{ h}$.

After withdrawal of clonidine the blood pressure gradually decreased and he showed the clinical picture of essential hypertension with neurogenic symptoms. He was then given propranolol 60 mg/day on day 18. On day 20 catecholamine concentrations had greatly decreased. Clinical signs gradually declined and disappeared around day 20 except for repeated episodes of flushing. His progress has been good on propranolol 120 mg/day, the blood pressure being within the range of 150/100 mm Hg.

Increases in catecholamine concentrations and blood pressure were closely related; the correlation coefficient was 0.74 for systolic pressure and 0.83 for diastolic pressure ($P < 0.001$).

Comment

Several reports have shown that the sudden withdrawal of long-term clonidine treatment may precipitate a hypertensive crisis^{2,3} accompanied by a rise in catecholamine concentrations, which may reach the levels found in pheochromocytoma.¹ This phenomenon might be prevented by gradual reduction of clonidine dosage.⁴ Nevertheless, a typical rebound phenomenon has been described after gradual withdrawal of clonidine,⁵ though the patient was also undergoing beta-blockade—a combination that may independently cause an important rise in blood pressure. Our patient also showed a typical rebound phenomenon when the daily dosage of clonidine was gradually reduced. Blood pressure and urinary catecholamine concentrations were greatly increased; the increases were statistically closely correlated. Our findings suggest that even gradual withdrawal of clonidine may precipitate a rebound phenomenon.

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¹ Hunyor, S N, *et al*, *British Medical Journal*, 1973, **2**, 209.

² Hansson, L, *et al*, *American Heart Journal*, 1973, **85**, 605.

³ Hökfelt, B, Hedeland, H, and Dymling, J F, *European Journal of Pharmacology*, 1970, **10**, 389.

⁴ Pettinger, W A, *New England Journal of Medicine*, 1975, **293**, 1179.

⁵ Cairns, S A, and Marshall, A J, *Lancet*, 1976, **1**, 368.

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