nitrogen mustard, and vincristine and on 1 June was discharged mentally well. She remained mentally well.

Comment

The symptoms and absence of organic brain disease in this patient supported a diagnosis of mania. The lack of personal or family history of affective psychosis, the recurrence of symptoms despite lithium carbonate and phenothiazines, and the time relation between the manic episodes and drug treatment suggest that the manic psychosis was unlikely to have been coincidental. Steroids were omitted from the drug regimen preceding the second episode and she was not taking other drugs likely to give psychiatric effects. Psychodynamically a "flight into mania" could be postulated as a reaction to learning about her grave physical illness, but during the episode she felt better than normal and the absence of affective symptoms before and after it makes this unlikely.

Procarbazine hydrochloride (isopropyl- α -(2-methylhydrazine)) is one of the monoamine oxidase inhibitors, long recognised as apt to provoke manic reactions.³ Though psychosis is a rare side effect of procarbazine, physicians should be aware of this and of its possible interaction with sympathomimetic agents to produce psychosis. Its antidepressant potential should be further explored.

We thank Dr I Chanarin for advice.

Requests for reprints should be sent to Dr M W P Carney.

¹ Mann AM, Hutchinson JL. Manic reactions associated with procarbazine hydrochloride therapy of Hodgkin's disease. *Can Med Assoc J* 1967;**97**:1350-3.

² De Conti RC. Procarbazine in the management of late Hodgkin's disease. *JAMA* 1971;**215**:927-30.

³ Schildkraut JJ. A catecholamine hypothesis of affective disorders: a review of supporting evidence. *Am J Psychiatry* 1965;**122**:509-22.

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Hypokalaemia induced by a combination of a beta-blocker and a thiazide

Preparations containing fixed-ratio combinations of a beta-blocker and a thiazide are being used to treat hypertension. The potential for hypokalaemia during such treatment has been understated, and we report a case of profound hypokalaemia induced by Sotazide (sotalol 160 mg and hydrochlorothiazide 25 mg).

Case report

A 55-year-old white woman was referred to the London Hospital hypertension clinic for management. She gave a three-year history of essential hypertension, and 10 weeks before referral Sotazide one tablet twice a day had been prescribed. At presentation she reported serious symptoms including lethargy and dizziness. On examination blood pressure was 150/98 mm Hg and pulse 64 beats/minute and grade I hypertensive retinopathy was noted. Further examination was normal. Investigation showed normal renal function and plasma potassium concentration of 2.4 mmol(mEq)/l. Sotazide was withdrawn, and the plasma potassium concentration returned to normal (3.8 mmol/l) over two weeks.

Triple treatment with propranolol 120 mg twice a day, Moduretic two tablets daily, and hydralazine 25 mg twice a day was required to control her blood pressure (134/90 mm Hg). Plasma potassium concentration remained normal at 3.5 mmol/l. Sotazide one tablet twice a day was then reintroduced to replace propranolol and Moduretic. Hypokalaemia developed (plasma potassium concentration 3.1 mmol/l after one week and 2.8 mmol/l after two weeks) with recurrence of her symptoms. Sotalol 160 mg twice a day was prescribed in place of Sotazide; the plasma potassium concentration returned to normal within one week (3.8 mmol/l) and she became asymptomatic.

All diuretic treatment was stopped and serum aldosterone concentration estimated, which was within the normal range, thus making unlikely the diagnosis of primary hyperaldosteronism (serum aldosterone concentration 226 pmol/l (8.1 ng/100 ml); normal range 150-500 pmol/l (5.4-1.8 ng/100 ml)).

Comment

Fixed-ratio combinations of beta-blocker and thiazide diuretics may reduce plasma potassium concentration profoundly, as is well recognised with thiazides alone.¹ Beta-blockers attenuate the fall in potassium concentration produced by thiazides,² and they raise plasma potassium concentrations by approximately 0.2 mmol/l.³ As thiazides cause a mean fall in plasma potassium concentration of about 0.6 mmol/l the combination of a beta-blocker and a thiazide would be expected to cause a fall of approximately 0.4 mmol/l. Indeed, this has been shown with the combination of sotalol and hydrochlorothiazide.⁴ Therefore, patients prescribed a fixed-ratio combination of a beta-blocker and a diuretic may still develop hypokalaemia and be at risk from its associated complications, which include an increased incidence of ventricular fibrillation and ventricular tachycardia after myocardial infarction⁵ as well as a general increase in non-specific morbidity, particularly in the elderly.

We think, therefore, that serum electrolyte concentrations should be closely monitored in all patients prescribed preparations combining a beta-blocker and a thiazide to avoid these and other consequences of hypokalaemia. Concurrent administration of a potassium-conserving diuretic or adequate potassium supplements may be appropriate.

¹ Morgan DB, Davidson C. Hypokalaemia and diuretics: an analysis of publications. *Br Med J* 1980;**280**:905-8.

² Sweet CS, Gaul SL. Attenuation of hydrochlorothiazide-induced hypokalaemia in dogs by a beta adrenergic blocking drug, Timolol. *Eur J Pharmacol* 1975;**2**:370-4.

³ Medical Research Council working party on mild to moderate hypertension. Randomised controlled trial of treatment for mild hypertension: design and pilot trial. *Br Med J* 1977;**ii**:1437-40.

⁴ Jaattela A. The combination of sotalol and hydrochlorothiazide in the treatment of hypertension. *J Clin Pharmacol* 1979;**19**:565-70.

⁵ Cole AG, Arkin D, Solomon R. Malignant ventricular dysrhythmias in myocardial infarction: the role of hypokalaemia. International Congress and Symposium series No 44. London: Royal Society of Medicine, 1981:47-53.

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Retroperitoneal fibrosis associated with metoprolol

Retroperitoneal fibrosis was first described in 1948. In a few cases an aetiological agent has been identified: analgesic abuse¹ and methysergide² have been implicated, as more recently have beta-adrenergic blockers including atenolol³ and oxprenolol.⁵ We report a case of retroperitoneal fibrosis in a patient who had been taking metoprolol for 11 months.

Case report

A 51-year-old labourer was referred to the outpatient clinic in February 1980 because of angina. Blood urea and creatinine concentrations were within the normal range. He had been taking slow-release metoprolol 200 mg daily and nifedipine 10 mg daily since September 1979. His drug treatment was altered to thrice-daily metoprolol 50 mg, nifedipine 10 mg, and isosorbide dinitrate 10 mg. In July 1980 he was admitted for coronary angiography and found to have a blood urea concentration of 23.3 mmol/l (140 mg/100 ml) and a creatinine concentration of 729 μ mol/l (8.24 mg/100 ml). Haemoglobin concentration was 12.8 g/dl, there was no abnormality on urine microscopy; and he was normotensive. Ultrasonography showed dilatation of the pelvic-calcic system in both kidneys; the upper portion of the right ureter appeared normal but the left ureter could not be seen. Cystoscopy showed no abnormality within the bladder, and the ureteric orifices appeared normal. Bilateral Chevasu (retrograde) ureterography disclosed the typical appearances of retroperitoneal fibrosis.

At operation retroperitoneal fibrosis was found affecting the left ureter for a distance of 5 cm and the right ureter for a distance of 2 cm. Bilateral ureterolysis was performed and the ureters fixed in a lateral position. A Silastic T tube was left as an intubated ureterostomy on the left. Fourteen days after operation his urea concentration was 7.9 mmol/l (47.4 mg/100 ml) and creatinine concentration 155 μ mol/l (1.75 mg/100 ml).

A month later he was readmitted complaining of fever, malaise, and lethargy. Intravenous pyelography disclosed a non-functioning left kidney, and retrograde studies on the left side showed a stricture of the ureter at the level of L4. Laparotomy confirmed continued blockage of the ureter by dense fibrous tissue and also a small abscess at the site of the T-tube ureterostomy. Left nephrectomy was performed. Histological examination of the kidney showed severe acute pyelonephritis secondary to ureteric obstruction. This was considered to be a complication of the T-tube ureterostomy.

Comment

While neither metoprolol nor nifedipine can be incriminated with certainty, the fact that several cases of retroperitoneal fibrosis have been associated with other beta-adrenergic blocking agents suggests the metoprolol may have been responsible for the condition in this case. The incidence of retroperitoneal fibrosis in the middle-aged, however, is still unknown, and, as beta-blocking drugs are now widely used to treat hypertension and angina, some "idiopathic" cases will inevitably occur in patients taking these drugs.

Finally, we emphasise that there appears to be no relation between retroperitoneal fibrosis and the fibrosing peritonitis that is an integral part of the mucocutaneous syndrome attributable to practolol.

We thank Mr R Hall for permission to report surgical details of this case, and both Mr Hall and Dr R Wilkinson for their help and advice in the management of this patient.

¹ Lewis CT, Molland EA, Marshall VR, Tresidder GC, Bland JP. Analgesic abuse, ureteric obstruction and retroperitoneal fibrosis. *Br Med J* 1975;iii:76-8.

² Graham JR. Methysergide for prevention of headache: experience in 500 patients over 3 years. *N Engl J Med* 1964;270:67-72.

³ Doherty CC, McGeown MG, Donaldson RA. Retroperitoneal fibrosis after treatment with atenolol. *Br Med J* 1978;ii:1786.

⁴ Johnson JN, McFarland JB. Retroperitoneal fibrosis associated with atenolol. *Br Med J* 1980;280:864.

⁵ McCluskey DR, Donaldson RA, McGeown MG. Oxprenolol and retroperitoneal fibrosis. *Br Med J* 1980;281:1459-60.

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Risk of hepatitis B virus infection in patients with eczema or psoriasis of the hand

Although hepatitis B virus is usually transmitted parenterally, many cases of infection occur in which overt parenteral contact with the virus cannot be shown. Faecal-oral spread of the virus is effectively blocked by an inhibitory substance present in the intestine and faeces of normal subjects.¹⁻⁴ To explain hepatitis B virus infection in the absence of overt parenteral exposure the "inapparent parenteral route" has been postulated. This term is used to indicate the penetration of virus into the organism through cutaneous and mucosal microlesions. Peroral infection with hepatitis B virus through microlesions in the oropharyngeal mucosa has been shown experimentally in chimpanzees.⁵

We think that skin lesions due to diseases such as psoriasis or eczema should also be considered as possible routes of entry for hepatitis B virus. The virus is present in biological fluids of carriers and could easily come in contact with lesions especially on the hands. We carried out a study to test this hypothesis.

Patients, methods, and results

Eighty-one patients with chronic eczema or psoriasis of the hand and with fissured lesions on the palm were divided into two groups. The first group (40 patients; 16 men and 24 women) had had eczema or psoriasis of the hand for less than two years. The second group (41 patients; 13 men and 28 women) had had the condition for more than two years. We chose 256 normal subjects (111 men and 145 women), comparable in sex, age, and socioeconomic background to serve as controls.

The patients and controls were tested for hepatitis B surface antigen (HBsAg), anti-HBs, and anti-hepatitis B core antigen by radioimmunoassay. Previous contact with hepatitis B virus was assumed if at least one of the markers tested for was present. The results were analysed by the χ^2 test (table). When the prevalence of HBsAg was considered a higher value was found in patients who had had skin lesions for more than two years. No significant difference between the groups was observed, however. When the prevalence of positivity for one or more markers including HBsAg was examined a significant difference was observed between controls and patients who had had skin lesions for more than two years.

Comment

These results show that a higher risk of infection with hepatitis B virus exists in patients with chronic skin diseases. This phenomenon is probably particularly evident in the Naples area, where the prevalence of HBsAg in the general population is high (4.18%). The environment is thus rich in hepatitis B virus, facilitating penetration of virus through lesions or microlesions of the skin. This is another example of transmission of infection by the "inapparent parenteral route."

Patients with chronic lesions of the hand should be considered to be at high risk for hepatitis B virus infection and high-priority candidates for inclusion in vaccination programmes. A higher prevalence of infection with non-A non-B hepatitis virus may also occur in these patients since the routes of transmission of B and non-A non-B viral hepatitis are similar.

¹ Piazza M, Di Stasio G, De Marco F. Why is serum hepatitis virus absent from faeces? *Br Med J* 1971;ii:772.

² Piazza M, Di Stasio G, Maio G, Marzano LA. Hepatitis B antigen inhibitor in human faeces and intestinal mucosa. *Br Med J* 1973;iii:334-7.

³ Piazza M, Cacciato L, Molinari V, et al. Presence of HBsAg in the bile of subjects with acute HBsAg viral hepatitis. *Pathologia et Microbiologia* 1975;43:307-16.

⁴ Mosley JW. Epidemiologic nomenclature for hepatitis B virus transmission. *Am J Epidemiol* 1980;111:261-2.

⁵ US Department of Health, Education and Welfare, Public Health Service, and Center for Disease Control. *Hepatitis surveillance. III. Hepatitis B transmission modes: evidence against enteric transmission.* Report No 41. Washington: DHEW, 1977:20-2.

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Prevalence of markers of hepatitis B virus infection in patients with hand eczema or psoriasis and in normal controls

	Mean $\pm$ SD time from first appearance of lesions (years)	No	Mean $\pm$ SD age (years)	Positive for HBsAg	Positive for one or more markers including HBsAg
Patients with skin lesions:					
<2 years	1.1 $\pm$ 0.1	40	29.4 $\pm$ 11.5	2 (5.0%)	17 (42.5%)
>2 years	4.9 $\pm$ 2.3	41	30.2 $\pm$ 10.7	4 (9.8%)	27 (65.9%)
Controls		256	28.3 $\pm$ 11.9	11 (4.3%)	101 (39.5%)

HBsAg = Hepatitis B surface antigen.