

criteria for a diagnosis of infectious mononucleosis. In a more recent report of an outbreak of the disease Dunnet (1963) described 80 cases; the diagnostic criteria used were stringent. Though almost all of the 80 cases had evidence of hepatic involvement and 13 (16%) had electrocardiographic changes, only a few had the radiological appearances of enlarged hilar lymph nodes and none had pulmonary lesions.

The present case satisfied the accepted diagnostic criteria for infectious mononucleosis. There was no direct evidence of infection other than of infectious mononucleosis, and the pulmonary changes coincided with the development and remission of the primary disease. It seems likely that the pulmonary opacities were due to foci of infiltration by mononuclear cells or atypical lymphocytes, as has been described in a minority of the few cases coming to necropsy (Ziegler, 1944; Allen and Kellner, 1947; Natvig, 1962). If these pulmonary opacities were indeed due to lymphocytic proliferation, we are reminded that the mechanism of proliferation and above all the limitation of lymphocytic prolifera-

tion in infectious mononucleosis is inadequately understood (Dameshek and Gunz, 1964).

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Hyperaldosteronism from Adrenal Carcinoma

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A case of primary aldosteronism caused by an adrenal carcinoma is reported. It reinforces the view of Spark and Melby (1968) that patients with aldosteronism due to an adrenal adenoma should be treated by removal of the primary lesion (whether adenoma or hyperplasia) rather than medically with spironolactone.

Case History

A man aged 35 was admitted to hospital with a history of pain, tenderness, and weakness in the muscles which had begun one month previously and gradually progressed until the day of admission, when he could not walk. Biceps, deltoids, quadriceps, and adductors and abductors of the hip were weak. He was unable to sit up from a lying position but was just able to lift both legs from the bed. The left knee jerk was obtainable only with reinforcement and the right ankle jerk was absent. Haemoglobin was 13 g/100 ml, W.B.C. 4,800/mm³, and E.S.R. 9 mm/hr (Westergren). Plasma electrolytes were sodium 145 mEq, potassium 1.7 mEq, and bicarbonate 40 mEq/l, and the blood urea was 22 mg/100 ml. Potassium supplements were given by mouth and intravenously on the first day to a total of 600 mEq without appreciable improvement. Continuing potassium supplements of from 250 to 400 mEq a day led to a gradual increase in serum potassium concentration and a return of muscle strength. X-ray examination of the chest and an intravenous pyelogram showed nothing abnormal.

Three months later aortography showed the left kidney to be displaced downwards and flattened. This depression of the kidney over a short period of time suggested a non-benign lesion of the left adrenal, and tomography showed a calcified opacity surrounded

by a soft tissue mass 12 cm in diameter displacing the kidney downwards and the spleen laterally. Further investigation showed aldosterone excretion rates of 48, 30, 43, and 25 µg a day (normal daily range 0-16 µg), and they were unaffected by changing dietary sodium and potassium. Excretion of 17-oxosteroids was normal but that of the 17-oxogenic steroids was 26-47 mg a day (normal daily range 5-20 mg). The normal rate of cortisol secretion suggested that some precursor of 17-oxogenic steroids other than cortisol was being produced. This explanation was supported by the abnormally high 11-oxygenation index of 1.1 (normal mean 0.32 ± 0.19 S.D.) and by the findings of high values for the excretion of pregnanetriol and tetrahydro-11-deoxycortisol. The excretion of 6-β-hydroxycortisol was found to be three times normal. Plasma renin activity was measured by radioimmunoassay for angiotensin 1. Normal range for our laboratory is 0.68 (± 0.25 S.D.) ng/ml/hr in the supine position on a diet containing 215 mEq of sodium and 50 mEq of potassium. The patient's level was 0.84 ng/ml/hr and rose normally on exercise to 1.25 ng/ml/hr.

At operation a large firm tumour with some cysts was removed. Postoperatively the patient made an excellent recovery. The serum potassium rose above 3.5 mEq/l. and stayed there without potassium supplements or spironolactone. The production of 17-oxogenic steroids and aldosterone returned to normal. The tumour measured 15 cm by 14 cm by 10 cm and weighed 1,000 g. It was partly solid, partly cystic, and contained yellow necrotic areas. Histologically it was an adrenal cortical carcinoma distinguished by pleomorphic cells with many mitoses and areas of necrosis.

Hypokalaemia did not recur after the operation but the patient had pulmonary metastases, which were controlled with cyclophosphamide. Presumably they were not secreting mineralocorticoid material.

Comment

There is little doubt that the adrenal neoplasm produced an excess of aldosterone leading to hypokalaemic weakness and virtual paralysis. That the neoplasm was a carcinoma is suggested by the infiltrative nature of the primary tumour, the histological picture of pleomorphic cells with many mitoses, and the appearance of pulmonary cannon-ball metastases. Clinical features of Cushing's syndrome which characterize most adrenal carcinomas were not pronounced. The increased excretion of 17-oxogenic steroids was due to metabolites of non-glucocorticoid precursors of cortisol, and the raised excretion of tetrahydro-11-deoxycortisol is a common feature of adrenal cortical carcinoma (Lipsett and Wilson, 1962). This, together with the increased aldosterone excretion rate, suggests that many biochemical pathways in the tumour were overactive. The only similar case was that reported by Foye and Feichtmeir (1955), who also described an adrenal carcinoma with sodium retention and potassium loss.

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There are other intriguing features of the present case. At no time was the patient hypertensive, in contrast to the usual situation in Conn's syndrome or bilateral adrenal hyperplasia. As Conn (1964) pointed out, however, the rise in pressure is variable and in the early stages may be minimal. The observations on blood pressure harmonize also with the measurements of plasma renin activity. In Conn's syndrome or bilateral hyperplasia renin activity is usually depressed, but in this patient the activity of the renal enzyme was normal. Again it must be postulated that the duration and degree of hyperaldosteronism were insufficient to depress plasma renin activity, offsetting the aldosterone effect. (Brunner *et al.*, 1970).

However the biochemical changes are explained, the possibility that a malignant adrenal lesion may be producing changes similar to those produced by a benign adenoma or bilateral hyperplasia makes it reasonable to advocate that detailed steroid studies should be done in all such patients; that the tumour, if present, should be located; and that if necessary one or both adrenal glands should be removed. Spironolactone has a place in the diagnosis and investigation

of primary aldosteronism but should not be used as a definitive treatment.

We thank Professor W. I. Cranston, under whose care the patient was at St. Thomas's Hospital; Mr. J. M. Pullan, who performed the adrenalectomy; Dr. Roger Hall, recently house physician to the medical unit; and the staff of the department of surgical pathology for the histological report. Dr. Lee acknowledges the generous help of the Lawson Tait Trust and the British Heart Foundation.

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Side Effects of Parenteral Long-acting Phenothiazines

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A patient on parenteral long-acting phenothiazines may present in the general hospital with unusual side effects causing considerable difficulties in diagnosis. In the present case the patient presented with a hypothalamic syndrome, the first to be reported, which adds weight to the hypothesis that this is one of the sites of action of these drugs in man.

Case History

A 24-year-old man had an eight-year history of intermittent addiction to drugs, though he had not taken any for four months before the present illness. He was admitted to a psychiatric hospital in March 1971 with auditory hallucinations and delusions. These symptoms failed to respond to sedation or electric convulsion therapy and treatment was started with fluphenazine decanoate (Modecate) intramuscularly. He received 50 mg of this drug initially and 100 mg a week later. The following day he discharged himself from hospital.

Two days later his limbs became increasingly stiff and difficult to use, his speech was slurred, he was unable to swallow, and he became increasingly drowsy. A week later he was readmitted to the general hospital in a stuporous state.

On examination he was found to be obese (weight 117 kg), febrile (37.6°C), and mute. After repeated stimuli he could be roused and would follow an observer with his eyes. When left alone he rapidly lapsed into sleep. He had pronounced tremor of the lips, tongue, and hands, with extrapyramidal rigidity in all limbs. There were no other abnormal physical signs. A provisional diagnosis of encephalitis was made. The diagnosis of catatonic stupor was considered but rejected because the clinical features were atypical. Intravenous amylobarbitone sodium failed to render him more accessible.

Routine investigations showed nothing abnormal apart from a

neutrophil leucocytosis and the presence of large amounts of fluphenazine breakdown products in the urine.

Over the next seven days his temperature and white cell count remained high, though no site of infection was found. He did not respond to antibiotic therapy. The hypothalamic syndrome characterized by disturbance of temperature regulation and drowsiness from which he could be roused only by repeated stimuli persisted for a week. His temperature then returned to normal. This improvement coincided with a fall in the concentration of fluphenazine breakdown products in the urine to negligible levels. The extrapyramidal signs responded to intramuscular procyclidine hydrochloride (Kemadrin).

Comment

The long-acting phenothiazine fluphenazine enanthate has been valuable in reducing the incidence of relapse in schizophrenic patients. Fluphenazine decanoate is a similar depot injectable neuroleptic with a longer duration of action.

This is the first clinical report of a hypothalamic syndrome induced inadvertently by long-acting phenothiazines. The patient also developed extrapyramidal features which are sometimes associated with long-acting phenothiazine treatment. These side effects are related to age, sex, and dose but in addition there is an individual sensitivity factor (Simpson, 1967), though in the present case the dose given was considerably greater than that usually recommended (Capstick, 1968). In some patients the normal dose has been greatly exceeded without ill effect (Kline, 1970).

This case report illustrates the diagnostic difficulties that may be encountered in patients receiving long-acting phenothiazines, particularly if on admission the past medical history is not known. Because these drugs are rarely prescribed in the general hospital setting their side effects are less well known and may escape recognition.

The diagnosis of long-acting phenothiazine-induced side effects should be considered in patients who present with stupor, disturbance of temperature regulation with no evidence of underlying infection, and extrapyramidal signs.

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