A post-mortem examination, carried out by Dr. Boczarow, pathologist at Staincliffe General Hospital, Dewsbury, showed congested brain and meninges. The brain was swollen and there were petechial spots present on the meninges. Cerebral vessels were also dilated. Heart, lungs and pleurae, and other viscera were normal. A specimen of hippocampus and of brain stem was sent to the Public Health Laboratory in London. Its report was as follows:

Egg culture of a pool of hippocampus and brain stem suspensions

No pocks produced on the chorioallantoic membranes of fertile eggs, therefore negative for vaccinia and herpes simplex viruses.

Brain

Hippocampus No Negri bodies seen in stained impression smears.

Mouse inoculation Intracerebral.

Hippocampus Mice sick with tremors and limb weakness leading to paralysis. 8 days post-inoculation impression smears of cut surface of brain—Negri bodies observed.

Conclusion

Rabies virus was present in the specimen of brain.

COMMENT

In this case the clinical diagnosis was difficult owing to unusual presentation simulating renal colic and urinary tract infection; also to failure in recognizing that the pain in the right leg was an important feature. Other difficulties were the absence of pharyngeal spasm in the early stage and the paucity of clinical signs until very late. The behaviour change suggested the possibility of hysteria. Also very late was the history of the dog-bite elicited from the father. The incubation period in this case was three months. In man it is usually at least two months after a bite on the leg.

I am grateful to Dr. G. B. Tait, Consultant Physician, Dewsbury General Hospital, for giving me permission to publish this case and to Dr. A. D. Macrae, of the Virus Reference Laboratory, Central Public Health Laboratory, Colindale, for confirming the diagnosis.

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Parkinsonism Associated With Alpha-methyldopa Therapy

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Among the less-common side-effects of alpha-methyldopa therapy are agranulocytosis (Hallwright, 1961), hepatotoxicity (Gillespie, 1960), spontaneous lactation (Pettinger *et al.*, 1963), hyperpyrexia (Montegriffo, 1963), and Parkinsonism (Grodén, 1963). The following is believed to be a further case of Parkinsonism attributable to the drug.

CASE REPORT

A man of 58 years was admitted to hospital with hypertensive encephalopathy. His blood-pressure was 300+/190 mm. Hg. E.C.G. showed left ventricular strain, and the blood urea varied between 65 and 85 mg./100 ml. He was treated with alpha-methyldopa, 500 mg. every six hours, on which his blood-pressure fell to 190/120. It subsequently rose to 220/140, and guanethidine was prescribed in addition, but as he felt well he failed to take it. Four months later he was readmitted because of "fainting" attacks. The blood-pressure was 240/120 mm. Hg, his expression was blank and immobile, cerebration slowed, and gait unsteady. The back of his neck was rigid, and he held his head in the air, untiringly and without support, even when he was lying down. Tone was increased in the arms, with cog-wheel rigidity. Co-ordination was impaired in all limbs. Reflexes were increased in the left arm and leg, and plantar responses were flexor. Investigation showed no evidence of collagen vascular disease.

The alpha methyldopa was withdrawn and his hypertension treated with parenteral pentolinium. Within five days his expression had become mobile, his cerebration quickened, the incoordination improved, and cog-wheel rigidity disappeared. At the time of this improvement adequate control of the hypertension had not been achieved, the blood-pressure averaging 220/135 mm. Hg when he was at rest in bed. Subsequent control was partially effected by

oral pempidine. The signs of Parkinsonism had completely resolved and did not recur.

Two other patients have been encountered who had less definite Parkinsonian features, which appeared to improve after withdrawal of methyldopa.

COMMENT

A case of Parkinsonism associated with alpha methyldopa therapy has previously been reported by Grodén (1963). In the present case it is reasonable to wonder whether the Parkinsonism could be due to arteriosclerotic cerebral disease. The Parkinsonism, however, regressed rapidly and completely a few days after alpha methyldopa was withdrawn, and it did not recur. The fact that reserpine and phenothiazine, both of which can cause Parkinsonism, act on similar metabolic pathways to those affected by alpha methyldopa was pointed out by Grodén. Parkinsonism due to reserpine, however, usually occurs only with the higher doses used in psychiatric practice, and rarely with the smaller doses employed for hypertension. Though the pharmacological action of alpha methyldopa differs from that of reserpine, the net effect of each is to cause depletion of tissue amine concentrations. It is not surprising, therefore, to find considerable similarity in effect between the two, both causing hypotension, bradycardia, oedema, and sedation, with side-effects that include depression, nightmares, stuffy nose, gastro-intestinal upsets, spontaneous lactation, and impotence. The occasional occurrence of Parkinsonism in association with alpha-methyldopa therapy as well as with reserpine is thus not unexpected.

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