# MEDULLARY INFARCTION — WAS IT DEPO-PROVERA?

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## INTRODUCTION

Recent studies in England and the United States indicate that the use of oral contraceptives is associated with an increased risk of deep vein thrombosis[1] pulmonary embolism, coronary thrombosis [1-3], cerebral thrombosis, ischaemia and haemorrhage[4]. Most strokes were thrombotic (42%) and the risk of stroke developing was 9.5 times greater than the control population. One of the striking findings in The Collaborative Group's Study for stroke in Young Women on contraceptives was the high proportion of women with strokes who smoked regularly. Other studies on women on oral contraceptives who developed coronary thrombosis have shown a 5 — 10 fold increased risk of thrombosis, when the individual smoked over 25 cigarettes per day[5]. In such studies, oestrogens alone or in combinations with progesterones have been incriminated. However such risks with Medroxyprogesterone (Depo-Provera) have not been reported. This parenteral long acting progesterone contraception has had previous report of neurological complications e.g. neuropathy, parasthesiae, depression and psychosis[6].

We report a possible relation between parenteral depo-provera and the subsequent development of medullary infarction in a patient who was a heavy smoker.

### History

The patient, a Chinese bar waitress aged 40 years, smoked 30 cigarettes daily for many years. She first saw her general practitioner in April 1979 for contraception and was given 150mg i.m. depo-provera. This was followed by a repeat injection in July. The next morning following the injection, she developed vertigo, and vomiting. When seen in the ENT Clinic of the hospital, the Rhinne and Weber's tests were normal and no abnormal neurological signs were present. The subsequent evening, her vertigo became more severe and she was admitted.

*Clinical examination* then showed that she was ill but well nourished and afebrile. BP 140/80 mm Hg, pulse 64 per min. Heart, Lungs and abdomen were normal. There was a (R) 12th nerve palsy with the tongue deviated to the right. No other neurological abnormalities were detected.

## INVESTIGATIONS

Blood counts, liver function tests, blood urea and electrolytes, ECG, chest x-ray, skull x-rays, urine analysis and urinary gonadotrophins test were normal.

She was treated symptomatically with intravenous fluids and stemetil and improved. On the 5th day, her vertigo and vomiting progressed when she developed more lower brain stem signs, of absent gag and swallowing reflexes, aphonia, cerebellar ataxia and titibation. That same day she had a grand mal fit and went into a coma. Despite intensive resuscitation, she remained in a coma and died on the 7th hospital day.

Autopsy findings were as follows:

A partial autopsy limited to the skull was performed. There was no evidence of external injury or fracture of the skull bone. The brain weighed 1190g. The vessels over the cerebral hemispheres were congested. There was bilateral uncal grooving and the cerebellar tonsils were prominent. The arteries of the circle of Willis and those around the brain stem were normal except for a short segment of the right vertebral artery which was mildly atherosclerotic. The lumen was however patent and no thrombus was present. Cut sections after perfusion revealed an area of softening associated with some haemorrhage involving the whole length of the right half of the medulla oblongata dorsal to the olivary nucleus (Fig. 1). The cephalic portion was more extensively involved than the caudal.

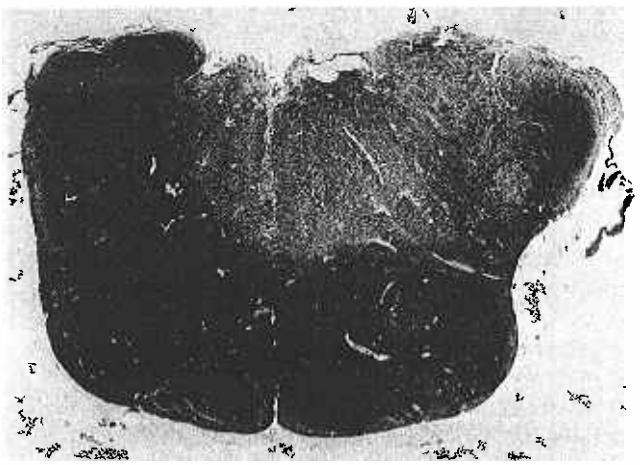

Figure 1. Whole microscopic section of the medulla oblongata at the level of the olivary nucleus showing a pale area of infarction dorsal to the olivary nucleus and extending to the floor of the fourth ventricle. It involves mainly the right half with some extension to the left side medially. Palmgren stain x 6.

Histological examination revealed an infarct undergoing liquefactive necrosis. There were extensive fragmentation of axons, degeneration of myelin and large numbers of foamy macrophages (Fig. 2). Perivascular cuffing with lymphocytes were seen in and around the area of necrosis. In a few small vessels, freshly deposited fibrin strands admixed with red blood cells were seen in the lumen. There was however no evidence of arteritis.

Examination of the rest of the brain revealed no other significant pathological findings.

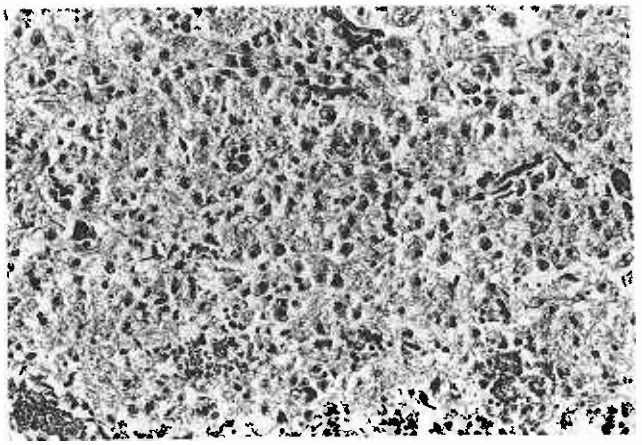

Figure 2. Microscopic section of the infarcted area showing liquefactive necrosis of the brain tissue and large numbers of foamy macrophages. H & E x 250.

## DISCUSSION

Although oestrogen and/or progesterone contraceptives have been used intensively for many years, the frequency of cerebral thrombosis developing in young women (especially Chinese) is rare. Most of the previous reports have shown that Caucasian females have a much higher risk than negro women. Though less reported, the rare adverse effects reported with Depo-provera are ectromelia, leukaemia, hypertension, embolism and colitis.

This patient was a heavy cigarette smoker and had no cerebral symptoms prior to the injection of depo-provera.

Her tinnitus developed about 12 hours following depo-provera suggesting a possible causative relationship. Depo-provera has not been previously reported to cause strokes even though strokes are 9.5 times more frequent in women on oral contraceptives who smoked heavily. The post mortem examination revealed minimal artherosclerosis of the vertebral artery but no thrombosis or occlusion. Could severe prolonged arterial spasm which is known to occur with heavy smoking from nicotine containing cigarettes be contributory towards the mechanism of infarction in this patient?[7] Similarly cigarette smoking and oral contraceptives are known to produce changes in plasma lipids which may enhance thrombosis. It may therefore be advisable for such patients to cease smoking or to use other forms of contraception in order to avoid this vascular complication.

## REFERENCES

1. United States Food and Drug Administration, Advisory Committee on Obstetrics and Gynaecology. Second Report on Oral Contraceptives, Washington D.C. Government Planning Office, August 1, 1969.
2. Inman W.H.W., Vessey M.P.: Investigations of deaths from pulmonary, coronary and cerebral thrombosis and embolism in women in child bearing age. Br. Med. J. 2 : 193 — 199, 1968.

3. Vessey M.P., Masi A.T., Arthes F.G. et al: Thromboembolism and oral contraceptives; an epidemiological case-control study. Am. J. Epidemiol. 90 : 365 — 380, 1969.
4. Collaborative Group for the Study of Stroke in Young Women: Oral Contraception and increase risk of cerebral ischaemia or thrombosis. New Eng. J. Med. 288: 871 — 878, 1973.
5. Cardiovascular Risks and Oral Contraceptives. Lancet 1: 1063, 1979.
6. W.H.O. International Monitoring of Adverse Drug Reaction (Ref 357), July — Sept 1968. Medroxy progesterone.
7. V. Kakkar: Peripheral vascular disease. Medicine (Ciba). Cardiovascular Diseases, Oct. 1979, 1118.